Guide to PHARMACOLOGY

GRAC database

Tutorial

Contents

Receptor family lists

Receptor pages

Ligand lists

Ligand pages

Search tools

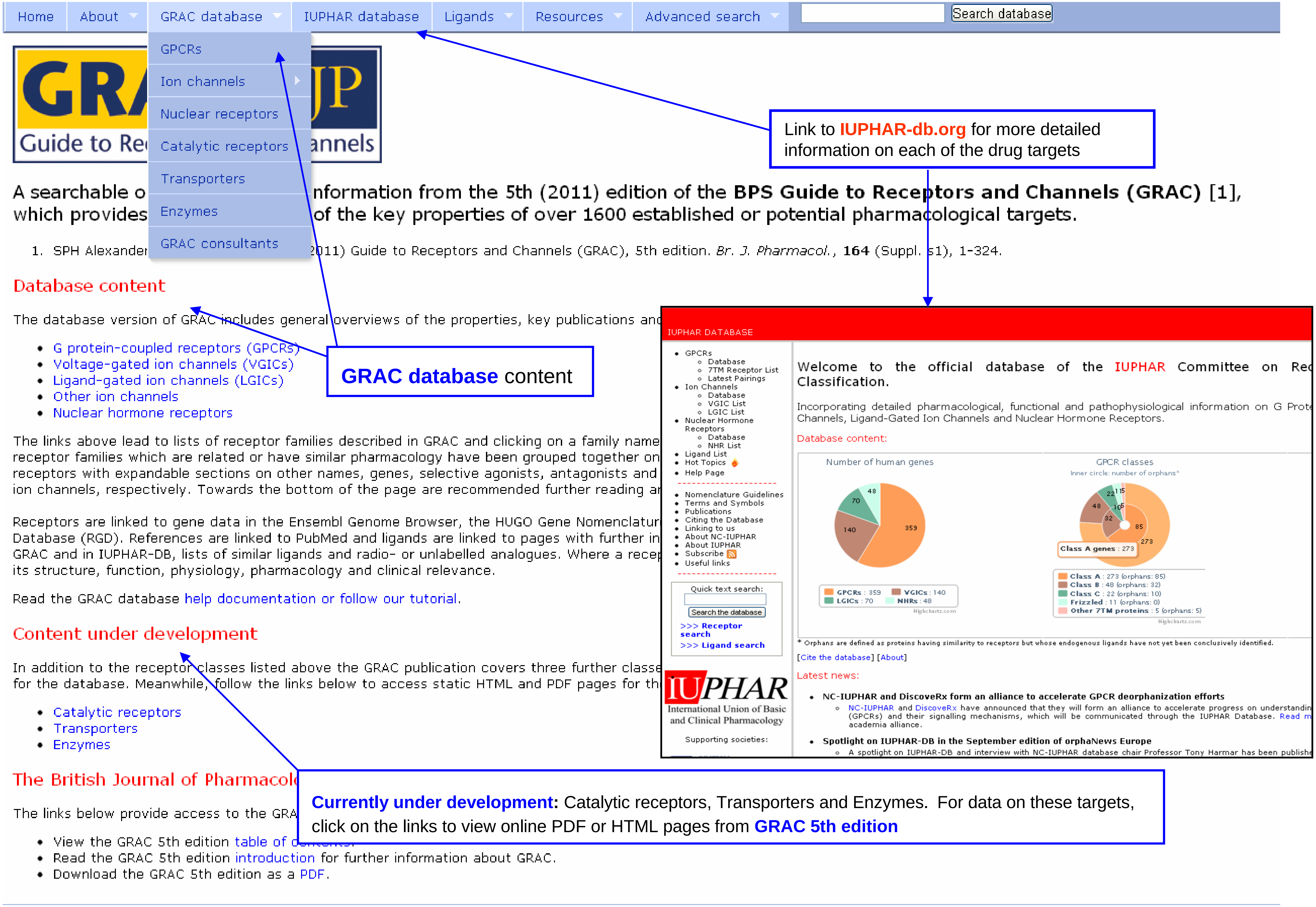
Database links

See the **About** pages for more information on the GRAC database, GRAC 5th Edition and the IUPHAR database

A PDF outlining pharmacological terms and symbols used in the GRAC database can be found at http://www.iuphar-db.org/termsAndSymbols.pdf

For definitions of terms used in this document and in the GRAC database go to the **Glossary** at the end of this document.

Email **enquiries@guidetopharmacology.org** *with comments/queries/suggestions about the* **Guide to PHARMACOLOGY**



Link to **IUPHAR-db.org** for more detailed information on each of the drug targets

A searchable o nformation from the 5th (2011) edition of the **BPS Guide to Receptors and Channels (GRAC)** [1], which provides of the key properties of over 1600 established or potential pharmacological targets.

1. SPH Alexander 2011) Guide to Receptors and Channels (GRAC), 5th edition. *Br. J. Pharmacol.*, **164** (Suppl. S1), 1-324.

Database content

The database version of GRAC includes general overviews of the properties, key publications and

- G protein-coupled receptors (GPCRs)
- Voltage-gated ion channels (VGICs)
- Ligand-gated ion channels (LGICs)
- Other ion channels
- Nuclear hormone receptors

GRAC database content

The links above lead to lists of receptor families described in GRAC and clicking on a family name receptor families which are related or have similar pharmacology have been grouped together on receptors with expandable sections on other names, genes, selective agonists, antagonists and ion channels, respectively. Towards the bottom of the page are recommended further reading ar

Receptors are linked to gene data in the Ensembl Genome Browser, the HUGO Gene Nomenclatur Database (RGD). References are linked to PubMed and ligands are linked to pages with further in GRAC and in IUPHAR-DB, lists of similar ligands and radio- or unlabelled analogues. Where a recep its structure, function, physiology, pharmacology and clinical relevance.

Read the GRAC database help documentation or follow our tutorial.

Content under development

In addition to the receptor classes listed above the GRAC publication covers three further classe for the database. Meanwhile, follow the links below to access static HTML and PDF pages for th

- Catalytic receptors
- Transporters
- Enzymes

The British Journal of Pharmacol

The links below provide access to the GRA

- View the GRAC 5th edition table of contents.
- Read the GRAC 5th edition introduction for further information about GRAC.
- Download the GRAC 5th edition as a PDF.

Currently under development: Catalytic receptors, Transporters and Enzymes. For data on these targets, click on the links to view online PDF or HTML pages from **GRAC 5th edition**

IUPHAR DATABASE

- GPCRs
  - Database
  - 7TM Receptor List
  - Latest Pairings
- Ion Channels
  - Database
  - VGIC List
  - LGIC List
- Nuclear Hormone Receptors
  - Database
  - NHR List
- Ligand List
- Hot Topics
- Help Page

- Nomenclature Guidelines
- Terms and Symbols
- Publications
- Citing the Database
- Linking to us
- About NC-IUPHAR
- About IUPHAR
- Subscribe
- Useful links

Welcome to the official database of the IUPHAR Committee on Rec Classification.

Incorporating detailed pharmacological, functional and pathophysiological information on G Prote Channels, Ligand-Gated Ion Channels and Nuclear Hormone Receptors.

Database content:

Number of human genes
48
70
140
359
GPCRs : 359
VGICs : 140
LGICs : 70
NHRs : 48
Highcharts.com
GPCR classes
Inner circle: number of orphans*
22
11
5
48
10
5
32
85
273
Class A genes : 273
Class A : 273 (orphans: 85)
Class B : 48 (orphans: 32)
Class C : 22 (orphans: 10)
Frizzled : 11 (orphans: 0)
Other 7TM proteins : 5 (orphans: 5)
Highcharts.com

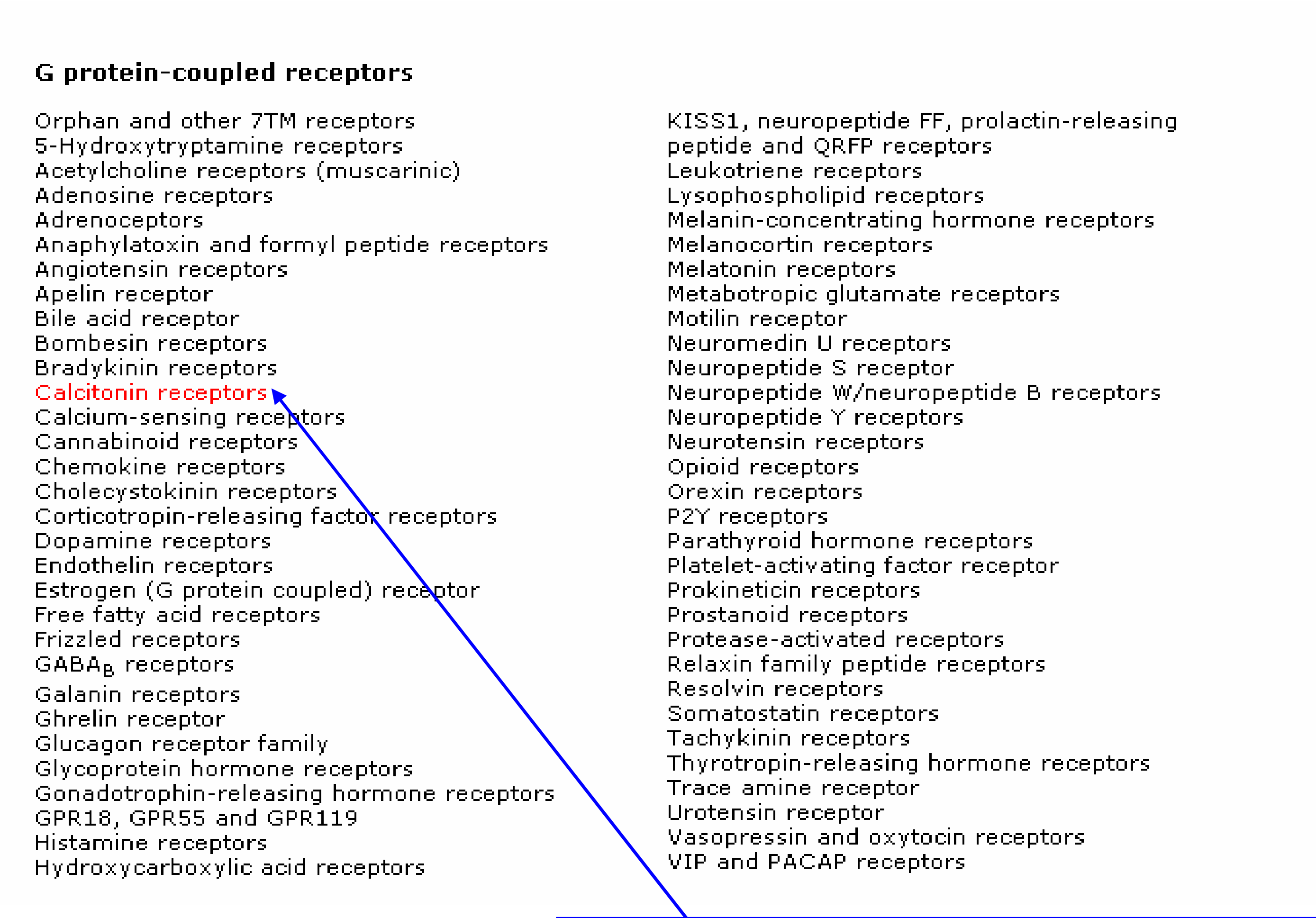
* Orphans are defined as proteins having similarity to receptors but whose endogenous ligands have not yet been conclusively identified.

[Cite the database] [About]

Latest news:

- **NC-IUPHAR and DiscoveRx form an alliance to accelerate GPCR deorphanization efforts**
  - NC-IUPHAR and DiscoveRx have announced that they will form an alliance to accelerate progress on understandin (GPCRs) and their signalling mechanisms, which will be communicated through the IUPHAR Database. Read m academia alliance.
- **Spotlight on IUPHAR-DB in the September edition of orphaNews Europe**
  - A spotlight on IUPHAR-DB and interview with NC-IUPHAR database chair Professor Tony Harmar has been publishe

List of receptor families: G protein-coupled receptors



G protein-coupled receptors

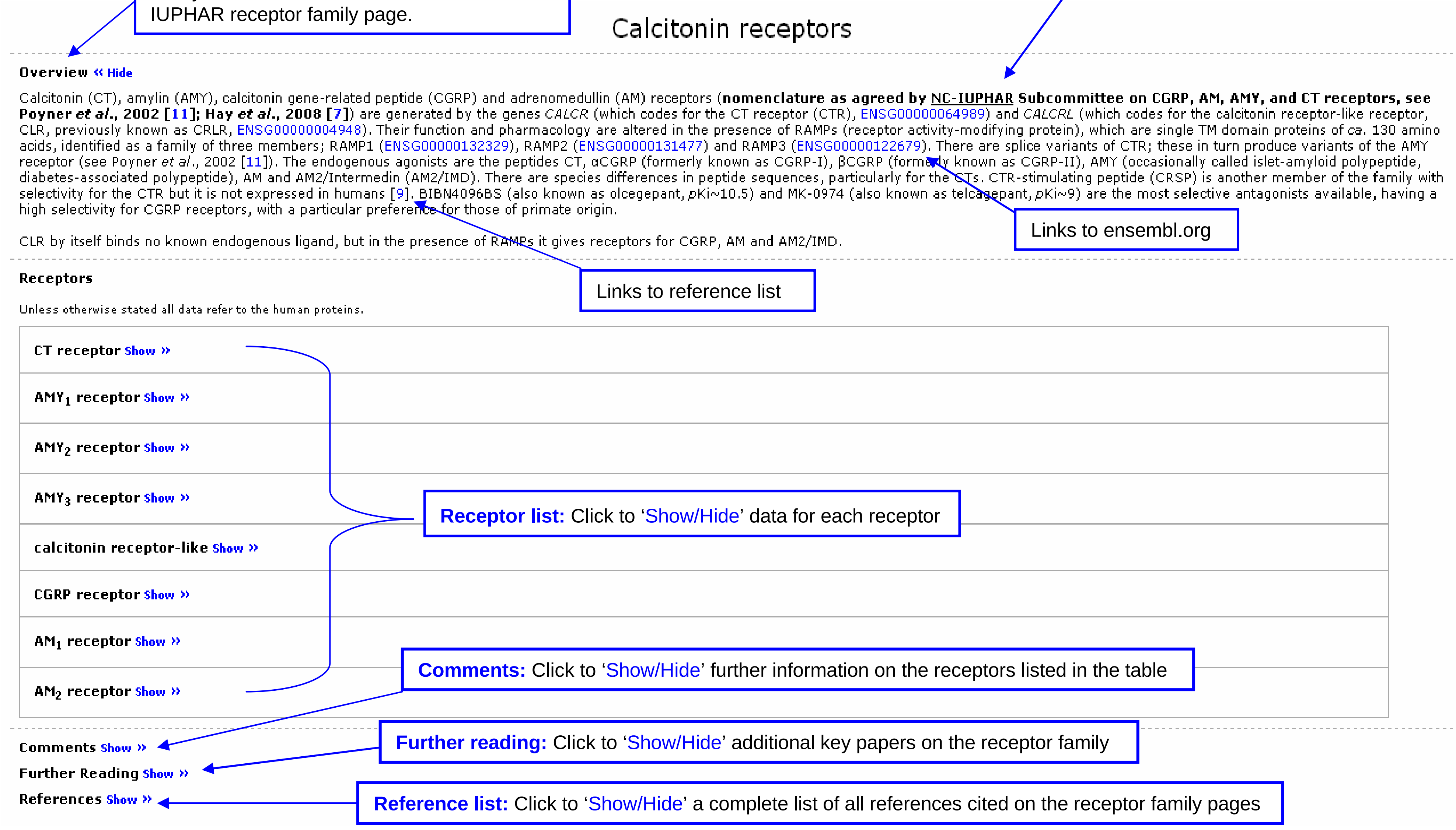
- Orphan and other 7TM receptors
- 5-Hydroxytryptamine receptors
- Acetylcholine receptors (muscarinic)
- Adenosine receptors
- Adrenoceptors
- Anaphylatoxin and formyl peptide receptors
- Angiotensin receptors
- Apelin receptor
- Bile acid receptor
- Bombesin receptors
- Bradykinin receptors
- Calcitonin receptors
- Calcium-sensing receptors
- Cannabinoid receptors
- Chemokine receptors
- Cholecystokinin receptors
- Corticotropin-releasing factor receptors
- Dopamine receptors
- Endothelin receptors
- Estrogen (G protein coupled) receptor
- Free fatty acid receptors
- Frizzled receptors
- GABA$_B$ receptors
- Galanin receptors
- Ghrelin receptor
- Glucagon receptor family
- Glycoprotein hormone receptors
- Gonadotrophin-releasing hormone receptors
- GPR18, GPR55 and GPR119
- Histamine receptors
- Hydroxycarboxylic acid receptors
- KISS1, neuropeptide FF, prolactin-releasing peptide and QRFP receptors
- Leukotriene receptors
- Lysophospholipid receptors
- Melanin-concentrating hormone receptors
- Melanocortin receptors
- Melatonin receptors
- Metabotropic glutamate receptors
- Motilin receptor
- Neuromedin U receptors
- Neuropeptide S receptor
- Neuropeptide W/neuropeptide B receptors
- Neuropeptide Y receptors
- Neurotensin receptors
- Opioid receptors
- Orexin receptors
- P2Y receptors
- Parathyroid hormone receptors
- Platelet-activating factor receptor
- Prokineticin receptors
- Prostanoid receptors
- Protease-activated receptors
- Relaxin family peptide receptors
- Resolvin receptors
- Somatostatin receptors
- Tachykinin receptors
- Thyrotropin-releasing hormone receptors
- Trace amine receptor
- Urotensin receptor
- Vasopressin and oxytocin receptors
- VIP and PACAP receptors

Each of the receptor families listed links to a **receptor family page**

Receptor family page

Overview: Brief introduction to the receptor family**.** For more detailed information see the IUPHAR receptor family page.

NC-IUPHAR review article on receptor nomenclature-
NC-IUPHAR reviews shown in bold in receptor family overviews



Calcitonin receptors

Overview « Hide

Calcitonin (CT), amylin (AMY), calcitonin gene-related peptide (CGRP) and adrenomedullin (AM) receptors (**nomenclature as agreed by NC-IUPHAR Subcommittee on CGRP, AM, AMY, and CT receptors, see Poyner *et al.*, 2002 [11]; Hay *et al.*, 2008 [7]**) are generated by the genes *CALCR* (which codes for the CT receptor (CTR), ENSG00000064989) and *CALCRL* (which codes for the calcitonin receptor-like receptor, CLR, previously known as CRLR, ENSG00000004948). Their function and pharmacology are altered in the presence of RAMPs (receptor activity-modifying protein), which are single TM domain proteins of *ca.* 130 amino acids, identified as a family of three members; RAMP1 (ENSG00000132329), RAMP2 (ENSG0000131477) and RAMP3 (ENSG00000122679). There are splice variants of CTR; these in turn produce variants of the AMY receptor (see Poyner *et al.*, 2002 [11]). The endogenous agonists are the peptides CT, αCGRP (formerly known as CGRP-I), βCGRP (formerly known as CGRP-II), AMY (occasionally called islet-amyloid polypeptide, diabetes-associated polypeptide), AM and AM2/Intermedin (AM2/IMD). There are species differences in peptide sequences, particularly for the CTs. CTR-stimulating peptide (CRSP) is another member of the family with selectivity for the CTR but it is not expressed in humans [9]. BIBN4096BS (also known as olcegepant, *p*Ki~10.5) and MK-0974 (also known as telcagepant, *p*Ki~9) are the most selective antagonists available, having a high selectivity for CGRP receptors, with a particular preference for those of primate origin.

CLR by itself binds no known endogenous ligand, but in the presence of RAMPs it gives receptors for CGRP, AM and AM2/IMD.

Links to ensembl.org

Links to reference list

Receptors

Unless otherwise stated all data refer to the human proteins.

CT receptor Show »
AMY$_1$ receptor Show »
AMY$_2$ receptor Show »
AMY$_3$ receptor Show »
calcitonin receptor-like Show »
CGRP receptor Show »
AM$_1$ receptor Show »
AM$_2$ receptor Show »

Receptor list: Click to 'Show/Hide' data for each receptor

Comments: Click to 'Show/Hide' further information on the receptors listed in the table

Comments Show »

Further Reading Show »

References Show »

Further reading: Click to 'Show/Hide' additional key papers on the receptor family

Reference list: Click to 'Show/Hide' a complete list of all references cited on the receptor family pages

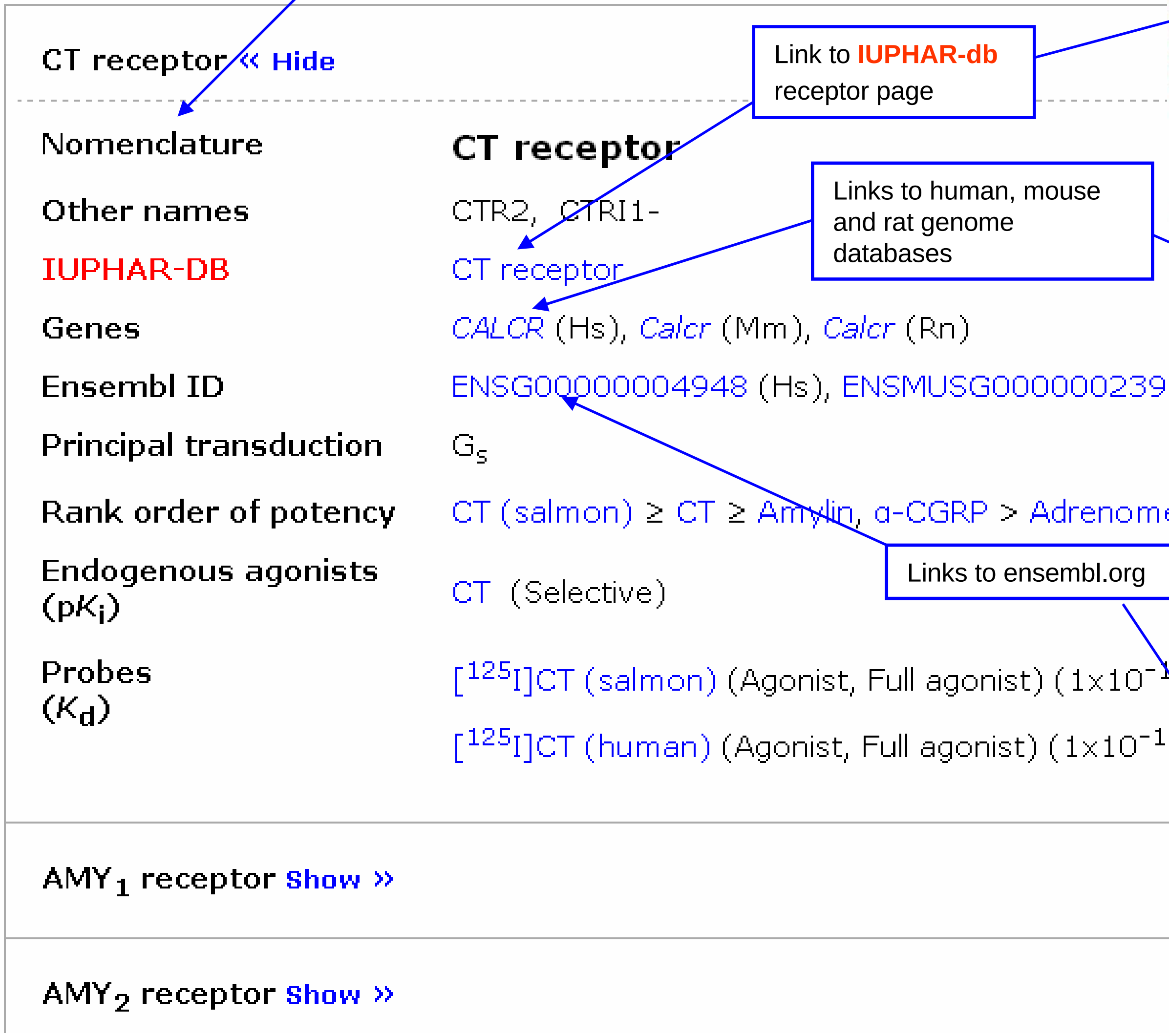
Receptor page

For a definition of nomenclature, see the **glossary**

Link to **IUPHAR-db** receptor page

Links to human, mouse and rat genome databases

Links to ensembl.org

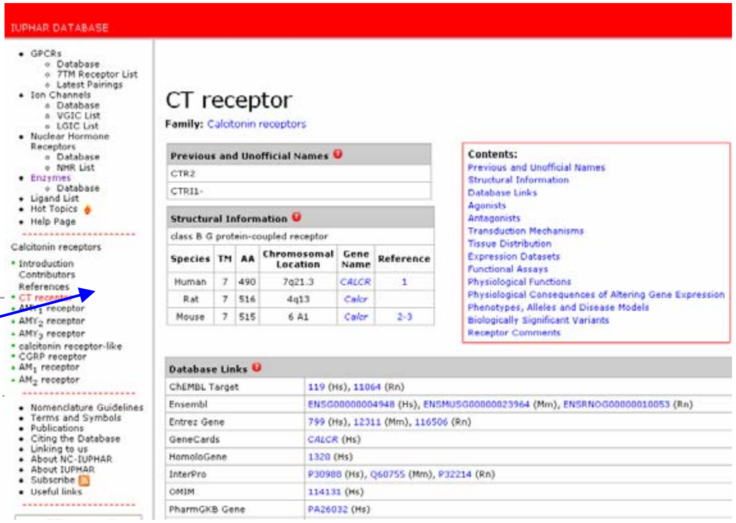


CT receptor « **Hide**

Nomenclature	**CT receptor**
Other names	CTR2, CTRI1-
IUPHAR-DB	CT receptor
Genes	*CALCR* (Hs), *Calcr* (Mm), *Calcr* (Rn)
Ensembl ID	ENSG00000004948 (Hs), ENSMUSG00000023964 (Mm), ENSR
Principal transduction	G_s
Rank order of potency	CT (salmon) ≥ CT ≥ Amylin, α-CGRP > Adrenomedullin, Adrenon
Endogenous agonists (pK_i)	CT (Selective)
Probes (K_d)	[^{125}I]CT (salmon) (Agonist, Full agonist) (1x10^{-10} M [^{125}I]CT (human) (Agonist, Full agonist) (1x10^{-10} –

AMY$_1$ receptor **Show »**

AMY$_2$ receptor **Show »**



IUPHAR DATABASE

- GPCRs
  - Database
  - 7TM Receptor List
  - Latest Pairings
- Ion Channels
  - Database
  - VGIC List
  - LGIC List
- Nuclear Hormone Receptors
  - Database
  - NHR List
- Enzymes
  - Database
- Ligand List
- Hot Topics
- Help Page

Calcitonin receptors

- Introduction
  Contributors
  References
- CT receptor
- AMY$_1$ receptor
- AMY$_2$ receptor
- AMY$_3$ receptor
- calcitonin receptor-like
- CGRP receptor
- AM$_1$ receptor
- AM$_2$ receptor

- Nomenclature Guidelines
- Terms and Symbols
- Publications
- Citing the Database
- Linking to us
- About NC-IUPHAR
- About IUPHAR
- Subscribe
- Useful links

CT receptor

Family: Calcitonin receptors

Previous and Unofficial Names
CTR2
CTRI1-

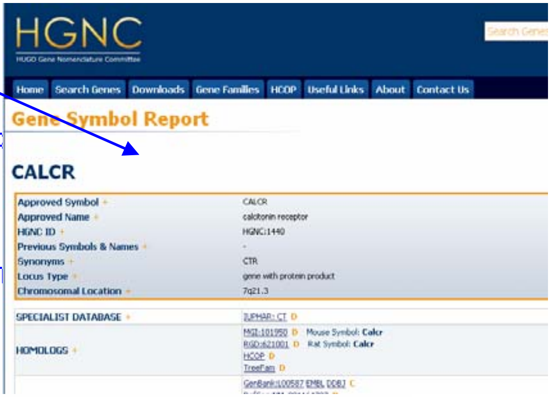
Structural Information

class B G protein-coupled receptor

Species	TM	AA	Chromosomal Location	Gene Name	Reference
Human	7	490	7q21.3	*CALCR*	1
Rat	7	516	4q13	*Calcr*	
Mouse	7	515	6 A1	*Calcr*	2-3

Contents:
Previous and Unofficial Names
Structural Information
Database Links
Agonists
Antagonists
Transduction Mechanisms
Tissue Distribution
Expression Datasets
Functional Assays
Physiological Functions
Physiological Consequences of Altering Gene Expression
Phenotypes, Alleles and Disease Models
Biologically Significant Variants
Receptor Comments

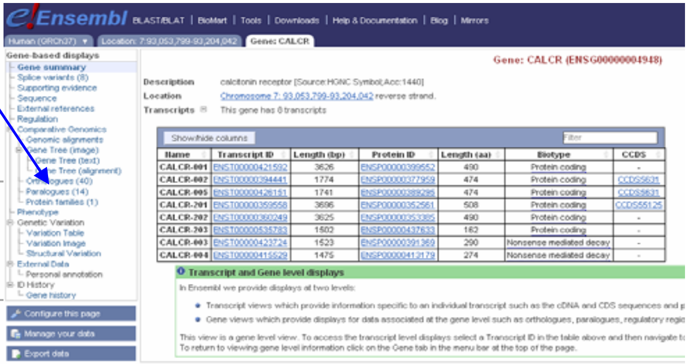
Database Links	
ChEMBL Target	119 (Hs), 11064 (Rn)
Ensembl	ENSG00000004948 (Hs), ENSMUSG00000023964 (Mm), ENSRNOG00000010053 (Rn)
Entrez Gene	799 (Hs), 12311 (Mm), 116506 (Rn)
GeneCards	*CALCR* (Hs)
HomoloGene	1320 (Hs)
InterPro	P30988 (Hs), Q60755 (Mm), P32214 (Rn)
OMIM	114131 (Hs)
PharmGKB Gene	PA26032 (Hs)



Gene Symbol Report

CALCR

Approved Symbol	CALCR
Approved Name	calcitonin receptor
HGNC ID	HGNC:1440
Previous Symbols & Names	-
Synonyms	CTR
Locus Type	gene with protein product
Chromosomal Location	7q21.3
SPECIALIST DATABASE	IUPHAR: CT
HOMOLOGS	MGI:101950 Mouse Symbol: **Calcr** RGD:621001 Rat Symbol: **Calcr** HCOP TreeFam
	GenBank:L00587 EMBL DDBJ



Gene: CALCR (ENSG00000004948)

Description	calcitonin receptor [Source:HGNC Symbol;Acc:1440]
Location	Chromosome 7: 93,053,799-93,204,042 reverse strand.
Transcripts	This gene has 8 transcripts

Name	Transcript ID	Length (bp)	Protein ID	Length (aa)	Biotype	CCDS
CALCR-001	ENST00000421592	3626	ENSP00000399552	490	Protein coding	-
CALCR-002	ENST00000394441	1774	ENSP00000377959	474	Protein coding	CCDS5631
CALCR-005	ENST00000426151	1741	ENSP00000389295	474	Protein coding	CCDS5631
CALCR-201	ENST00000359558	3696	ENSP00000352561	508	Protein coding	CCDS55125
CALCR-202	ENST00000360249	3625	ENSP00000353385	490	Protein coding	-
CALCR-203	ENST00000535783	1502	ENSP00000437633	162	Protein coding	-
CALCR-003	ENST00000423724	1523	ENSP00000391369	290	Nonsense mediated decay	-
CALCR-004	ENST00000415529	1475	ENSP00000413179	274	Nonsense mediated decay	-

Transcript and Gene level displays

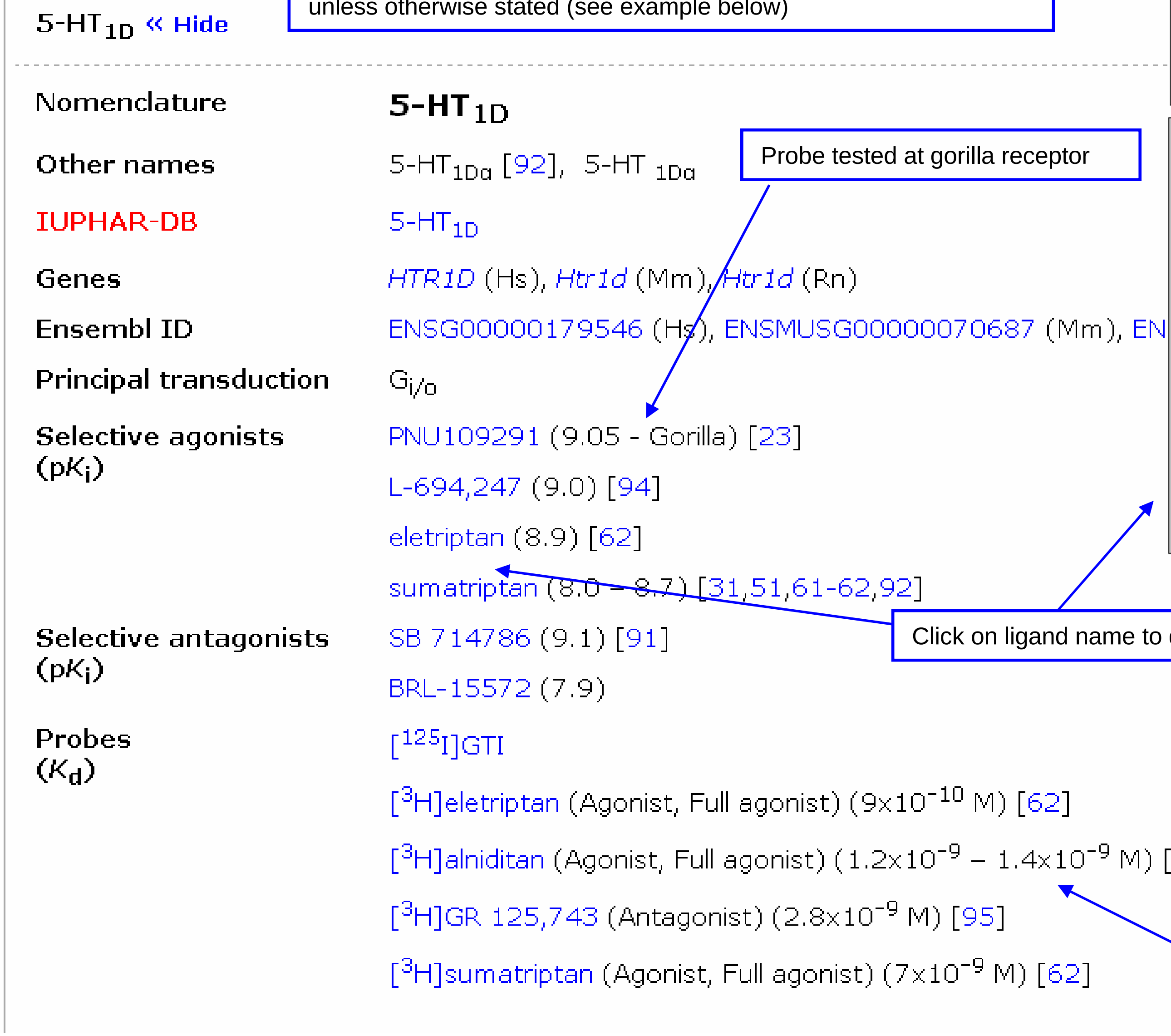
In Ensembl we provide displays at two levels:

- Transcript views which provide information specific to an individual transcript such as the cDNA and CDS sequences and p
- Gene views which provide displays for data associated at the gene level such as orthologues, paralogues, regulatory regio

This view is a gene level view. To access the transcript level displays select a Transcript ID in the table above and then navigate t
To return to viewing gene level information click on the Gene tab in the menu bar at the top of the page.

Receptor page

All data listed in the receptor tables refers to the **human** protein unless otherwise stated (see example below)



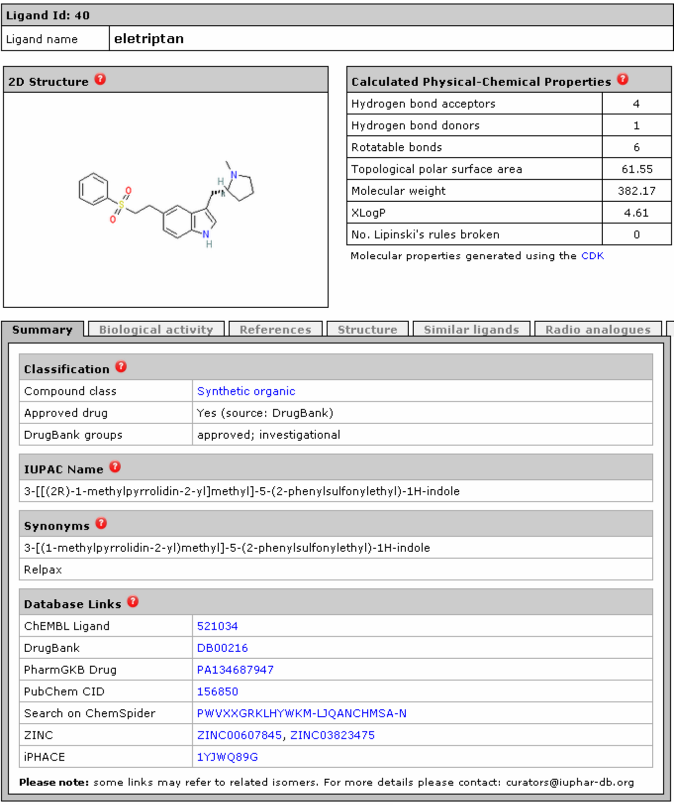
5-HT$_{1D}$ « Hide

Nomenclature	**5-HT$_{1D}$**
Other names	5-HT$_{1D\alpha}$ [92], 5-HT $_{1D\alpha}$
IUPHAR-DB	5-HT$_{1D}$
Genes	*HTR1D* (Hs), *Htr1d* (Mm), *Htr1d* (Rn)
Ensembl ID	ENSG00000179546 (Hs), ENSMUSG00000070687 (Mm), EN
Principal transduction	G$_{i/o}$
Selective agonists (pK_i)	PNU109291 (9.05 - Gorilla) [23] L-694,247 (9.0) [94] eletriptan (8.9) [62] sumatriptan (8.0 – 8.7) [31,51,61-62,92]
Selective antagonists (pK_i)	SB 714786 (9.1) [91] BRL-15572 (7.9)
Probes (K_d)	$[^{125}I]$GTI $[^{3}H]$eletriptan (Agonist, Full agonist) (9×10^{-10} M) [62] $[^{3}H]$alniditan (Agonist, Full agonist) (1.2×10^{-9} – 1.4×10^{-9} M) [50] $[^{3}H]$GR 125,743 (Antagonist) (2.8×10^{-9} M) [95] $[^{3}H]$sumatriptan (Agonist, Full agonist) (7×10^{-9} M) [62]

Probe tested at gorilla receptor

Click on ligand name to display the **GRAC ligand page**

GRAC activity data, with link to reference



Ligand Id: 40	
Ligand name	**eletriptan**

2D Structure

Calculated Physical-Chemical Properties	
Hydrogen bond acceptors	4
Hydrogen bond donors	1
Rotatable bonds	6
Topological polar surface area	61.55
Molecular weight	382.17
XLogP	4.61
No. Lipinski's rules broken	0

Molecular properties generated using the CDK

Classification	
Compound class	Synthetic organic
Approved drug	Yes (source: DrugBank)
DrugBank groups	approved; investigational

IUPAC Name

3-[[(2R)-1-methylpyrrolidin-2-yl]methyl]-5-(2-phenylsulfonylethyl)-1H-indole

Synonyms

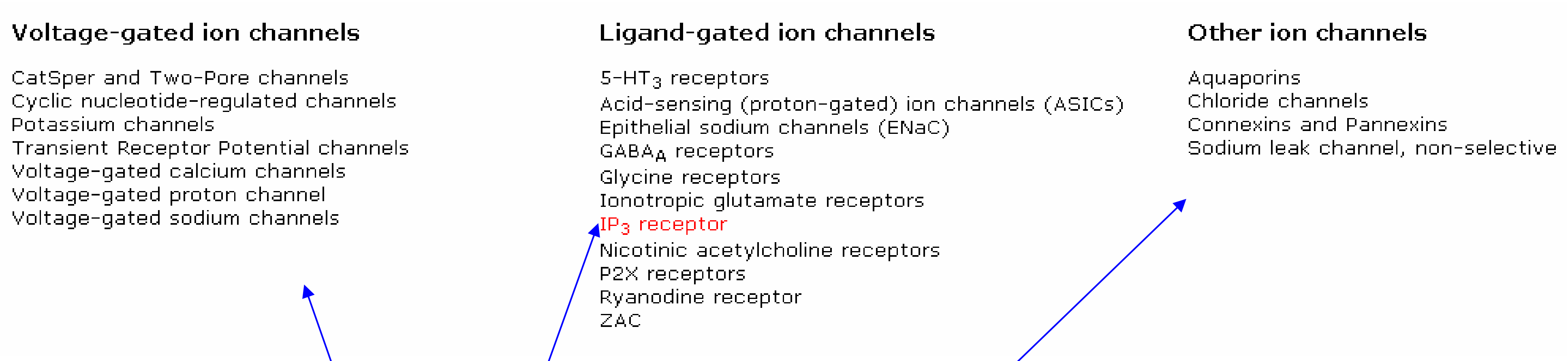
3-[(1-methylpyrrolidin-2-yl)methyl]-5-(2-phenylsulfonylethyl)-1H-indole

Relpax

Database Links	
ChEMBL Ligand	521034
DrugBank	DB00216
PharmGKB Drug	PA134687947
PubChem CID	156850
Search on ChemSpider	PWVXXGRKLHYWKM-LJQANCHMSA-N
ZINC	ZINC00607845, ZINC03823475
iPHACE	1YJWQ89G

Please note: some links may refer to related isomers. For more details please contact: curators@iuphar-db.org

Ion Channels: Receptor family list



Voltage-gated ion channels

CatSper and Two-Pore channels
Cyclic nucleotide-regulated channels
Potassium channels
Transient Receptor Potential channels
Voltage-gated calcium channels
Voltage-gated proton channel
Voltage-gated sodium channels

Ligand-gated ion channels

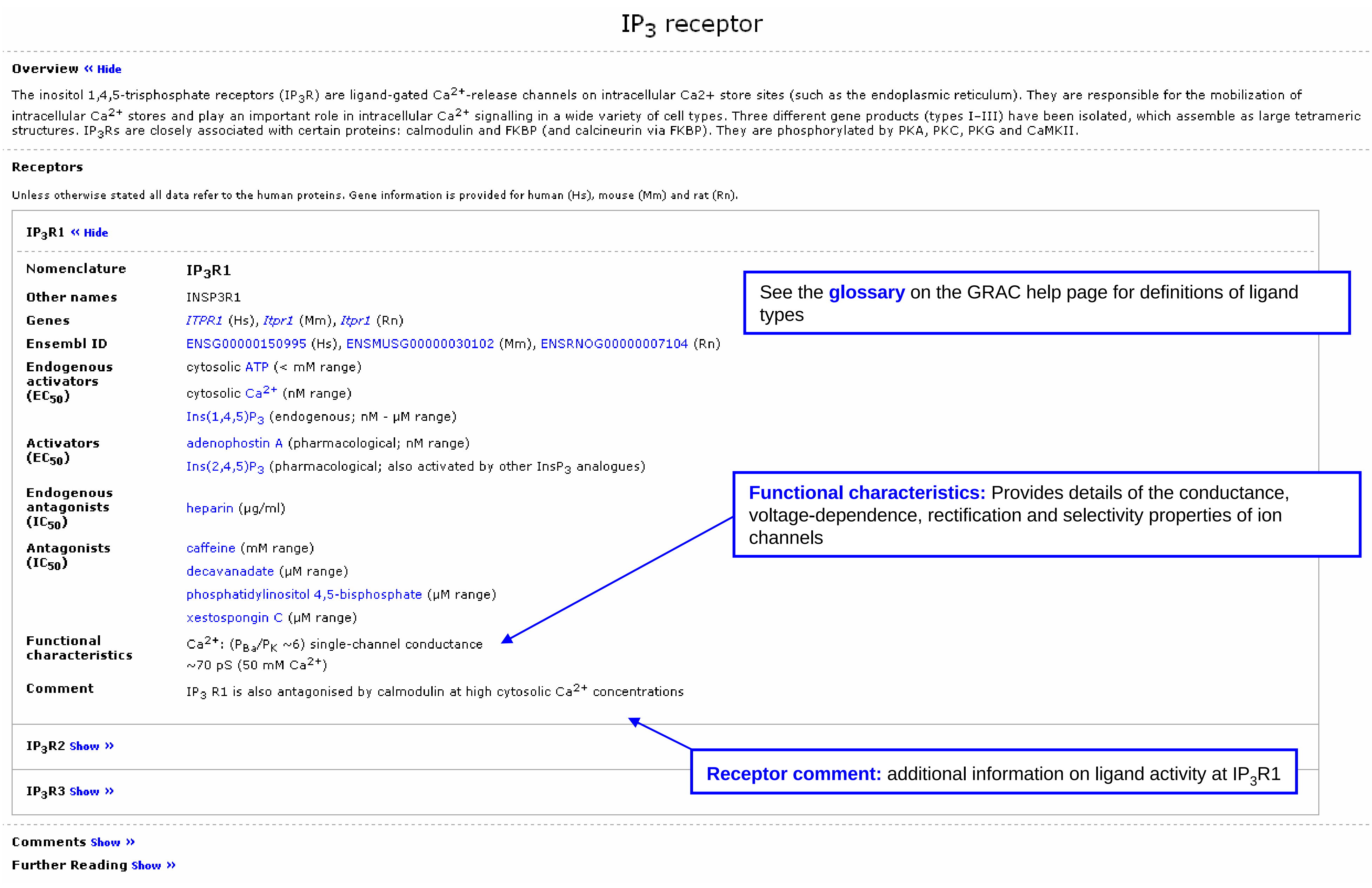
5-HT$_3$ receptors
Acid-sensing (proton-gated) ion channels (ASICs)
Epithelial sodium channels (ENaC)
GABA$_A$ receptors
Glycine receptors
Ionotropic glutamate receptors
IP$_3$ receptor
Nicotinic acetylcholine receptors
P2X receptors
Ryanodine receptor
ZAC

Other ion channels

Aquaporins
Chloride channels
Connexins and Pannexins
Sodium leak channel, non-selective

Ion channel receptor families are grouped according to gating regulator
Click on the receptor family name to view the receptor pages

Receptor page: IP$_3$R1 receptor, IP$_3$ receptor family



IP$_3$ receptor

Overview « Hide

The inositol 1,4,5-trisphosphate receptors (IP$_3$R) are ligand-gated Ca^{2+}-release channels on intracellular Ca2+ store sites (such as the endoplasmic reticulum). They are responsible for the mobilization of intracellular Ca^{2+} stores and play an important role in intracellular Ca^{2+} signalling in a wide variety of cell types. Three different gene products (types I–III) have been isolated, which assemble as large tetrameric structures. IP$_3$Rs are closely associated with certain proteins: calmodulin and FKBP (and calcineurin via FKBP). They are phosphorylated by PKA, PKC, PKG and CaMKII.

Receptors

Unless otherwise stated all data refer to the human proteins. Gene information is provided for human (Hs), mouse (Mm) and rat (Rn).

IP$_3$R1 « Hide

Nomenclature	**IP$_3$R1**
Other names	INSP3R1
Genes	*ITPR1* (Hs), *Itpr1* (Mm), *Itpr1* (Rn)
Ensembl ID	ENSG00000150995 (Hs), ENSMUSG00000030102 (Mm), ENSRNOG00000007104 (Rn)
Endogenous activators (EC$_{50}$)	cytosolic ATP (< mM range) cytosolic Ca^{2+} (nM range) Ins(1,4,5)P$_3$ (endogenous; nM - μM range)
Activators (EC$_{50}$)	adenophostin A (pharmacological; nM range) Ins(2,4,5)P$_3$ (pharmacological; also activated by other InsP$_3$ analogues)
Endogenous antagonists (IC$_{50}$)	heparin (μg/ml)
Antagonists (IC$_{50}$)	caffeine (mM range) decavanadate (μM range) phosphatidylinositol 4,5-bisphosphate (μM range) xestospongin C (μM range)
Functional characteristics	Ca^{2+}: (P$_{Ba}$/P$_K$ ~6) single-channel conductance ~70 pS (50 mM Ca^{2+})
Comment	IP$_3$ R1 is also antagonised by calmodulin at high cytosolic Ca^{2+} concentrations

IP$_3$R2 Show »

IP$_3$R3 Show »

Comments Show »

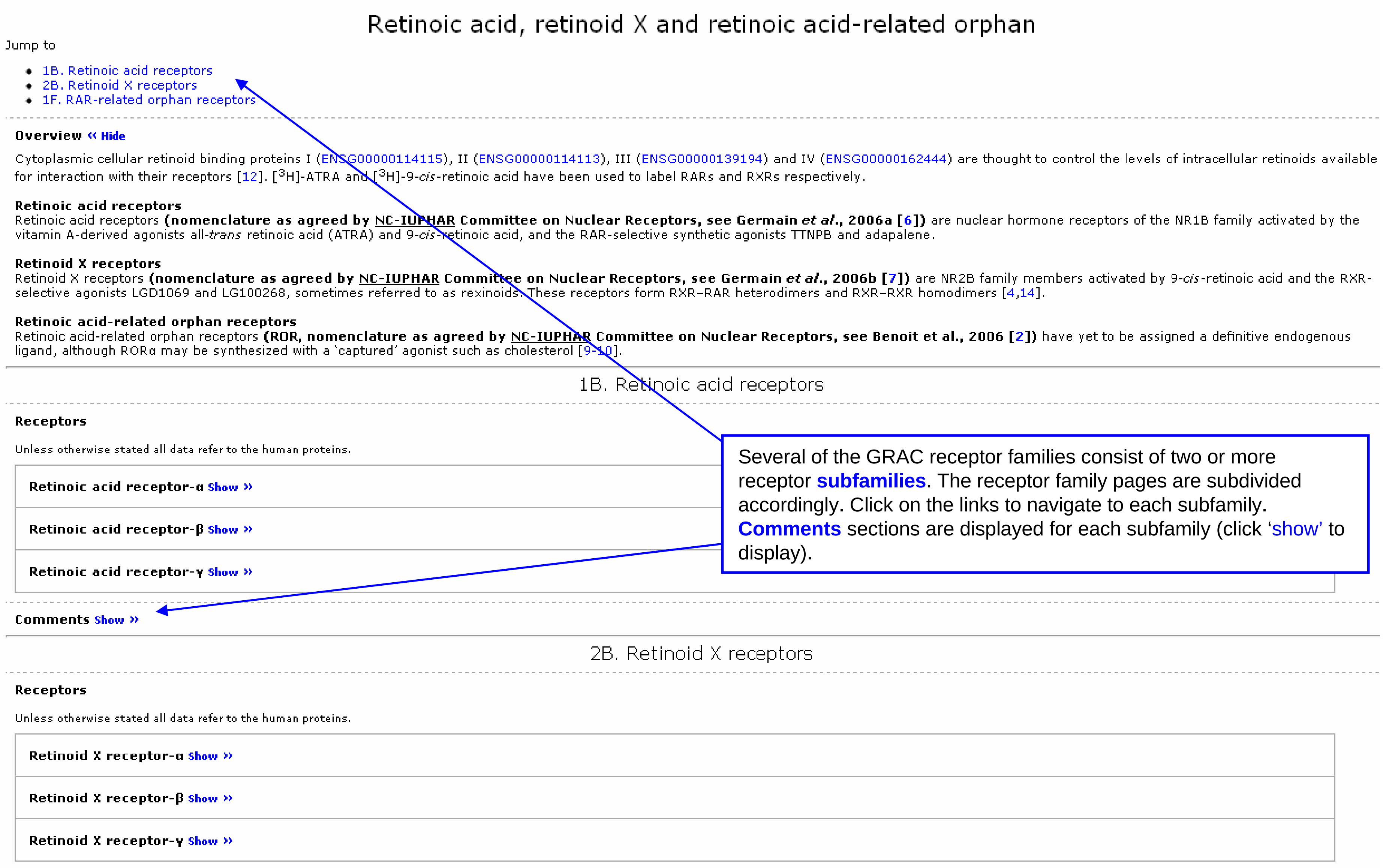
Further Reading Show »

See the **glossary** on the GRAC help page for definitions of ligand types

Functional characteristics: Provides details of the conductance, voltage-dependence, rectification and selectivity properties of ion channels

Receptor comment: additional information on ligand activity at IP$_3$R1

Nuclear receptors: Retinoic acid, retinoid X and retinoic acid-related orphan receptor family page



Retinoic acid, retinoid X and retinoic acid-related orphan

Jump to

- 1B. Retinoic acid receptors
- 2B. Retinoid X receptors
- 1F. RAR-related orphan receptors

Overview « Hide

Cytoplasmic cellular retinoid binding proteins I (ENSG00000114115), II (ENSG00000114113), III (ENSG00000139194) and IV (ENSG00000162444) are thought to control the levels of intracellular retinoids available for interaction with their receptors [12]. [^{3}H]-ATRA and [^{3}H]-9-*cis*-retinoic acid have been used to label RARs and RXRs respectively.

Retinoic acid receptors
Retinoic acid receptors **(nomenclature as agreed by NC-IUPHAR Committee on Nuclear Receptors, see Germain *et al*., 2006a [6])** are nuclear hormone receptors of the NR1B family activated by the vitamin A-derived agonists all-*trans* retinoic acid (ATRA) and 9-*cis*-retinoic acid, and the RAR-selective synthetic agonists TTNPB and adapalene.

Retinoid X receptors
Retinoid X receptors **(nomenclature as agreed by NC-IUPHAR Committee on Nuclear Receptors, see Germain *et al*., 2006b [7])** are NR2B family members activated by 9-*cis*-retinoic acid and the RXR-selective agonists LGD1069 and LG100268, sometimes referred to as rexinoids. These receptors form RXR–RAR heterodimers and RXR–RXR homodimers [4,14].

Retinoic acid-related orphan receptors
Retinoic acid-related orphan receptors **(ROR, nomenclature as agreed by NC-IUPHAR Committee on Nuclear Receptors, see Benoit et al., 2006 [2])** have yet to be assigned a definitive endogenous ligand, although RORα may be synthesized with a 'captured' agonist such as cholesterol [9-10].

1B. Retinoic acid receptors

Receptors

Unless otherwise stated all data refer to the human proteins.

Retinoic acid receptor-α Show »

Retinoic acid receptor-β Show »

Retinoic acid receptor-γ Show »

Comments Show »

2B. Retinoid X receptors

Receptors

Unless otherwise stated all data refer to the human proteins.

Retinoid X receptor-α Show »

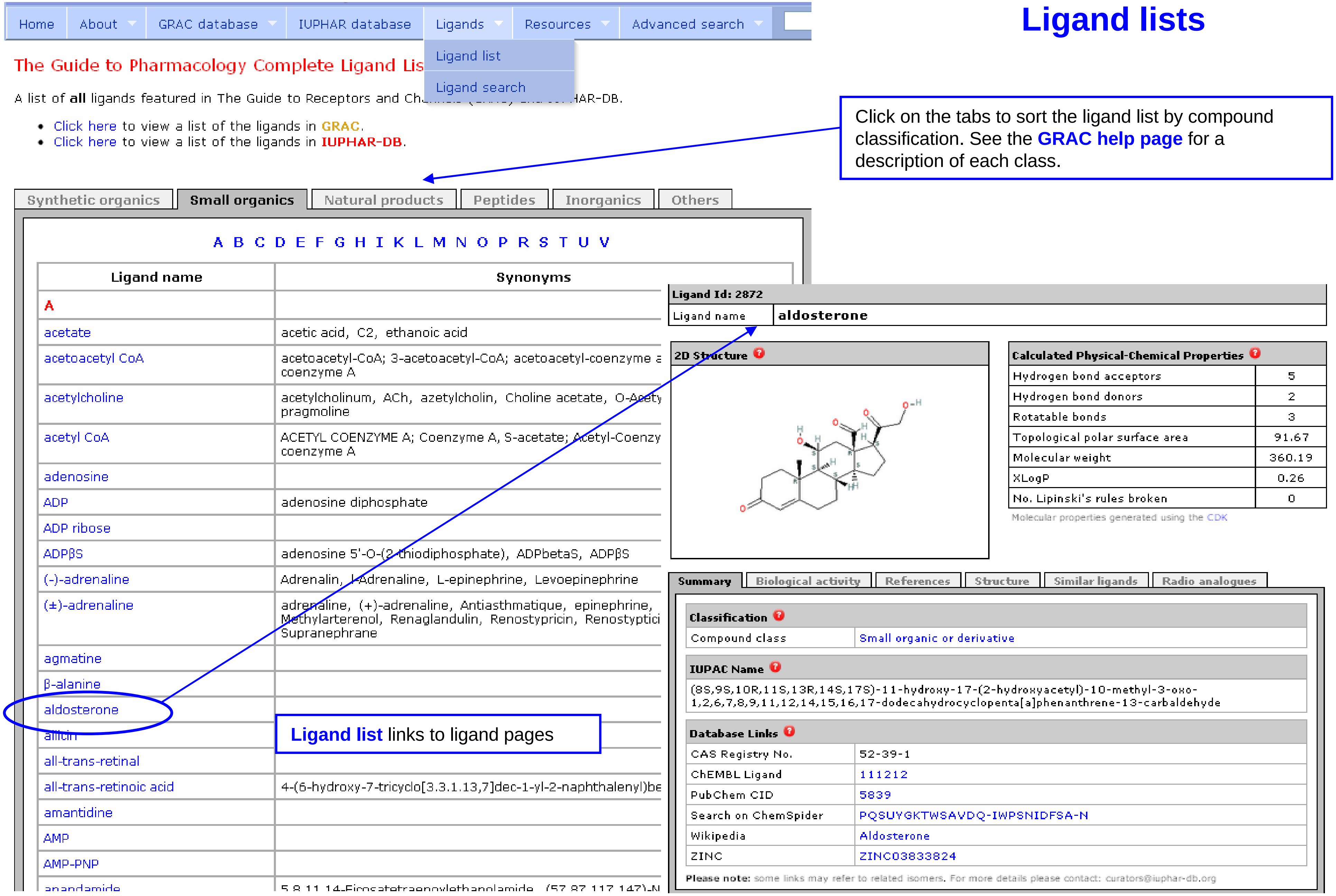
Retinoid X receptor-β Show »

Retinoid X receptor-γ Show »

Several of the GRAC receptor families consist of two or more receptor **subfamilies**. The receptor family pages are subdivided accordingly. Click on the links to navigate to each subfamily. **Comments** sections are displayed for each subfamily (click 'show' to display).

Ligand lists

Click on the tabs to sort the ligand list by compound classification. See the **GRAC help page** for a description of each class.



The Guide to Pharmacology Complete Ligand Lis

A list of **all** ligands featured in The Guide to Receptors and Ch HAR-DB.

- Click here to view a list of the ligands in GRAC.
- Click here to view a list of the ligands in IUPHAR-DB.

Ligand name	Synonyms
A	
acetate	acetic acid, C2, ethanoic acid
acetoacetyl CoA	acetoacetyl-CoA; 3-acetoacetyl-CoA; acetoacetyl-coenzyme a coenzyme A
acetylcholine	acetylcholinum, ACh, azetylcholin, Choline acetate, O-Acety pragmoline
acetyl CoA	ACETYL COENZYME A; Coenzyme A, S-acetate; Acetyl-Coenzy coenzyme A
adenosine	
ADP	adenosine diphosphate
ADP ribose	
ADPβS	adenosine 5'-O-(2-thiodiphosphate), ADPbetaS, ADPβS
(-)-adrenaline	Adrenalin, l-Adrenaline, L-epinephrine, Levoepinephrine
(±)-adrenaline	adrenaline, (+)-adrenaline, Antiasthmatique, epinephrine, Methylarterenol, Renaglandulin, Renostypricin, Renostyptici Supranephrane
agmatine	
β-alanine	
aldosterone	
allicin	
all-trans-retinal	
all-trans-retinoic acid	4-(6-hydroxy-7-tricyclo[3.3.1.13,7]dec-1-yl-2-naphthalenyl)be
amantidine	
AMP	
AMP-PNP	
anandamide	5,8,11,14-Eicosatetraenoylethanolamide, (5Z,8Z,11Z,14Z)-N

Ligand list links to ligand pages

Ligand Id: 2872

Ligand name	**aldosterone**

2D Structure

Calculated Physical-Chemical Properties	
Hydrogen bond acceptors	5
Hydrogen bond donors	2
Rotatable bonds	3
Topological polar surface area	91.67
Molecular weight	360.19
XLogP	0.26
No. Lipinski's rules broken	0

Molecular properties generated using the CDK

Classification	
Compound class	Small organic or derivative

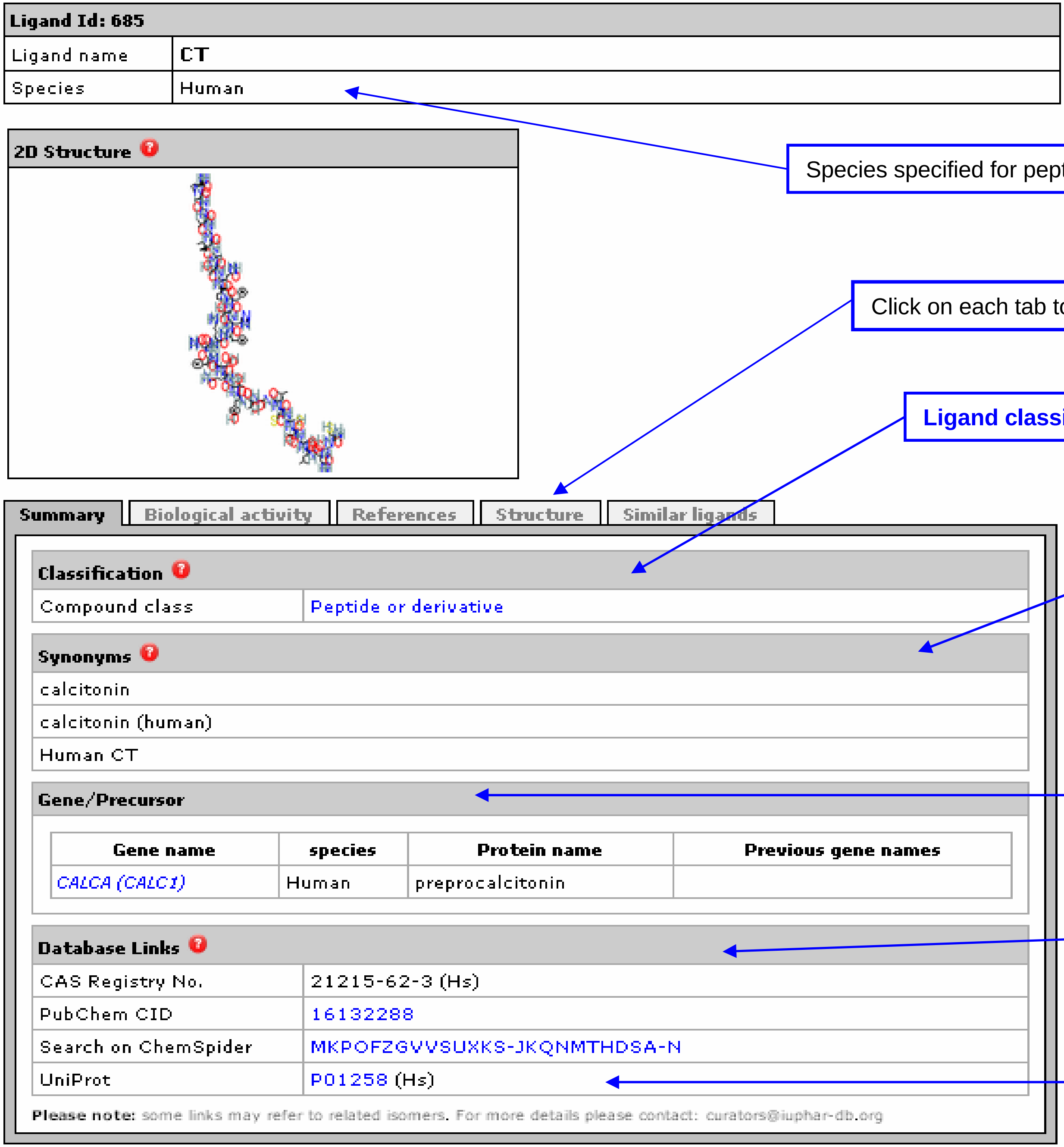
IUPAC Name

(8S,9S,10R,11S,13R,14S,17S)-11-hydroxy-17-(2-hydroxyacetyl)-10-methyl-3-oxo-1,2,6,7,8,9,11,12,14,15,16,17-dodecahydrocyclopenta[a]phenanthrene-13-carbaldehyde

Database Links	
CAS Registry No.	52-39-1
ChEMBL Ligand	111212
PubChem CID	5839
Search on ChemSpider	PQSUYGKTWSAVDQ-IWPSNIDFSA-N
Wikipedia	Aldosterone
ZINC	ZINC03833824

Please note: some links may refer to related isomers. For more details please contact: curators@iuphar-db.org

Example of a peptide ligand Summary page



Ligand Id: 685	
Ligand name	**CT**
Species	Human

2D Structure

Summary | Biological activity | References | Structure | Similar ligands

Classification	
Compound class	Peptide or derivative

Synonyms
calcitonin
calcitonin (human)
Human CT

Gene/Precursor

Gene name	species	Protein name	Previous gene names
CALCA (CALC1)	Human	preprocalcitonin	

Database Links	
CAS Registry No.	21215-62-3 (Hs)
PubChem CID	16132288
Search on ChemSpider	MKPOFZGVVSUXKS-JKQNMTHDSA-N
UniProt	P01258 (Hs)

Please note: some links may refer to related isomers. For more details please contact: curators@iuphar-db.org

Species specified for peptide ligands

Click on each tab to display ligand data/information

Ligand classification- see **glossary** for further explanation

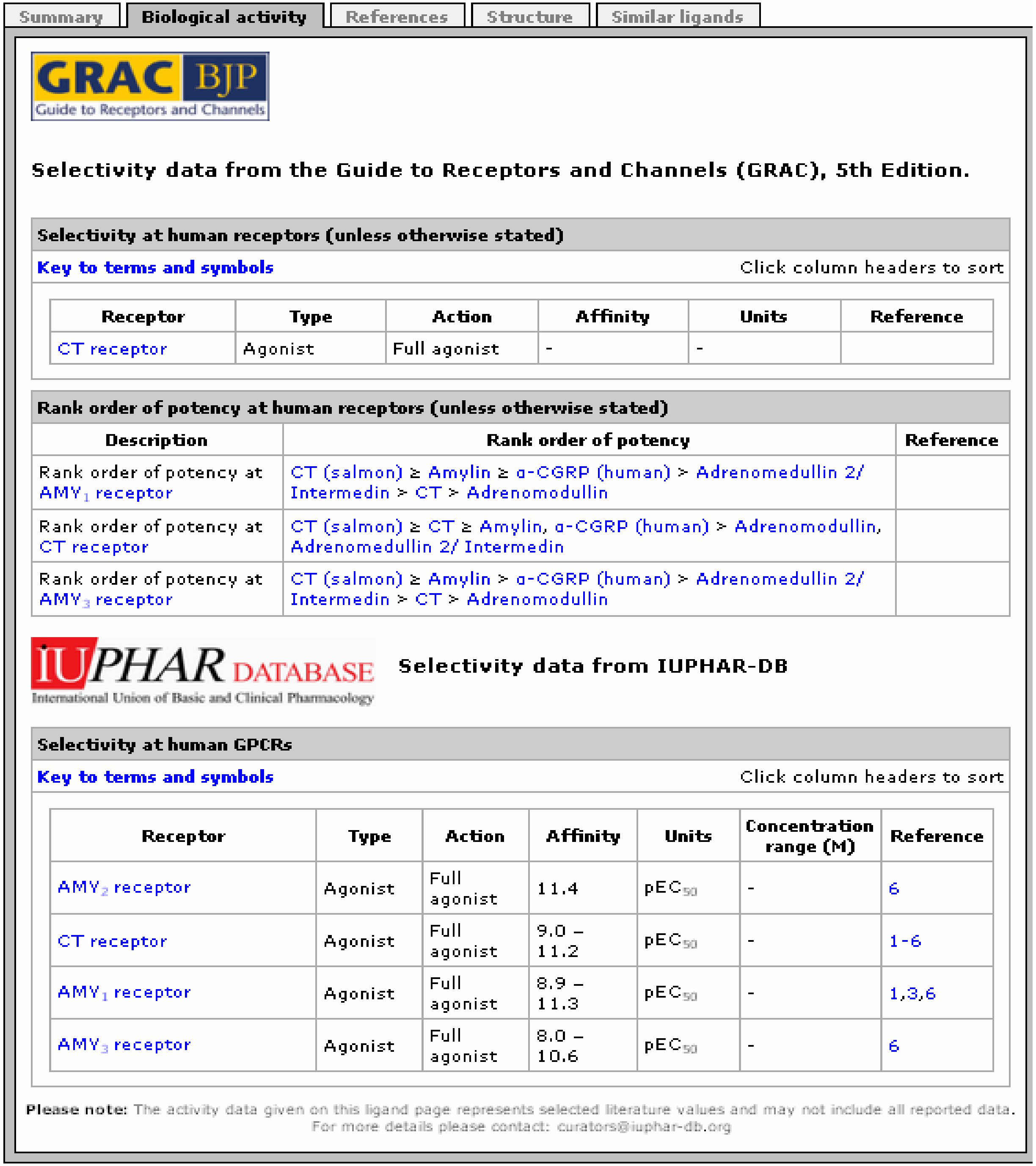
Synonyms: Alternative names for the ligand. Some may be systematic names. These may be used as search terms.

Link to the **HGNC database** for more information on the **gene**

Databases: Click to link to other relevant resources including genomic and chemical databases for further data on the ligand.

Link to **UniProt** for more information on the protein and its precursor

Ligand page: CT (Biological activity)



Selectivity data from the Guide to Receptors and Channels (GRAC), 5th Edition.

Selectivity at human receptors (unless otherwise stated)

Key to terms and symbols Click column headers to sort

Receptor	Type	Action	Affinity	Units	Reference
CT receptor	Agonist	Full agonist	-	-	

Rank order of potency at human receptors (unless otherwise stated)

Description	Rank order of potency	Reference
Rank order of potency at AMY_1 receptor	CT (salmon) ≥ Amylin ≥ α-CGRP (human) > Adrenomedullin 2/ Intermedin > CT > Adrenomodullin	
Rank order of potency at CT receptor	CT (salmon) ≥ CT ≥ Amylin, α-CGRP (human) > Adrenomodullin, Adrenomedullin 2/ Intermedin	
Rank order of potency at AMY_3 receptor	CT (salmon) ≥ Amylin > α-CGRP (human) > Adrenomedullin 2/ Intermedin > CT > Adrenomodullin	

Selectivity data from IUPHAR-DB

Selectivity at human GPCRs

Key to terms and symbols Click column headers to sort

Receptor	Type	Action	Affinity	Units	Concentration range (M)	Reference
AMY_2 receptor	Agonist	Full agonist	11.4	pEC_{50}	-	6
CT receptor	Agonist	Full agonist	9.0 – 11.2	pEC_{50}	-	1-6
AMY_1 receptor	Agonist	Full agonist	8.9 – 11.3	pEC_{50}	-	1,3,6
AMY_3 receptor	Agonist	Full agonist	8.0 – 10.6	pEC_{50}	-	6

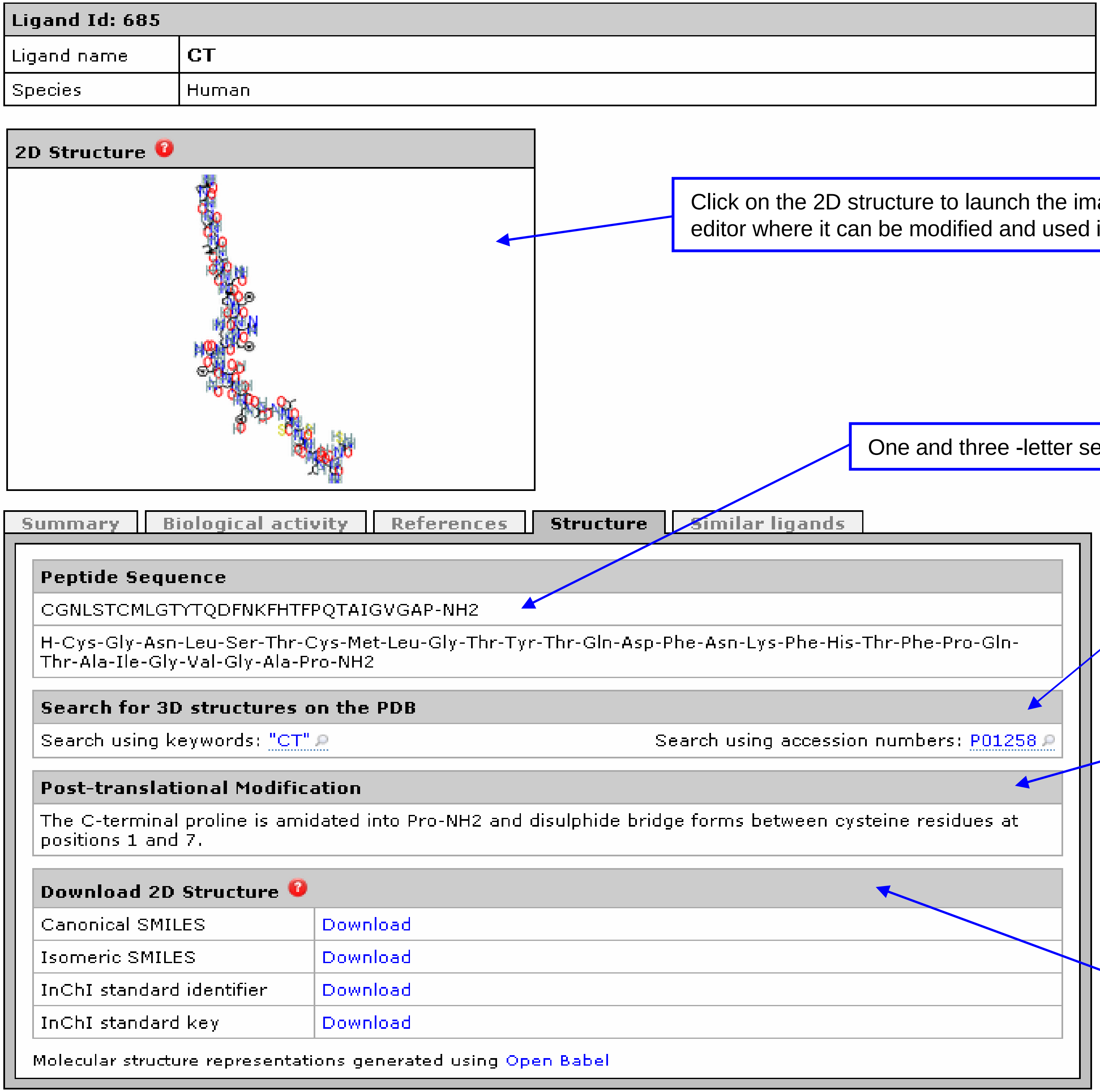
Please note: The activity data given on this ligand page represents selected literature values and may not include all reported data. For more details please contact: curators@iuphar-db.org

GRAC database activity data: Table displays all activity data for the ligand from the Guide to Receptors and Channels 5th edition

IUPHAR database activity data: Table displays all activity data for the ligand from the IUPHAR database. As the table indicates, CT is an agonist at several of the receptors from the calcitonin family.

Click on the receptor name in the table to link to the IUPHAR receptor page.

Ligand page: CT (Structural information)



Ligand Id: 685	
Ligand name	**CT**
Species	Human

2D Structure

Peptide Sequence

CGNLSTCMLGTYTQDFNKFHTFPQTAIGVGAP-NH2

H-Cys-Gly-Asn-Leu-Ser-Thr-Cys-Met-Leu-Gly-Thr-Tyr-Thr-Gln-Asp-Phe-Asn-Lys-Phe-His-Thr-Phe-Pro-Gln-Thr-Ala-Ile-Gly-Val-Gly-Ala-Pro-NH2

Search for 3D structures on the PDB

Search using keywords: "CT"   Search using accession numbers: P01258

Post-translational Modification

The C-terminal proline is amidated into Pro-NH2 and disulphide bridge forms between cysteine residues at positions 1 and 7.

Download 2D Structure	
Canonical SMILES	Download
Isomeric SMILES	Download
InChI standard identifier	Download
InChI standard key	Download

Molecular structure representations generated using Open Babel

Click on the 2D structure to launch the image in the MarvinSketch chemical editor where it can be modified and used in structure-based searches

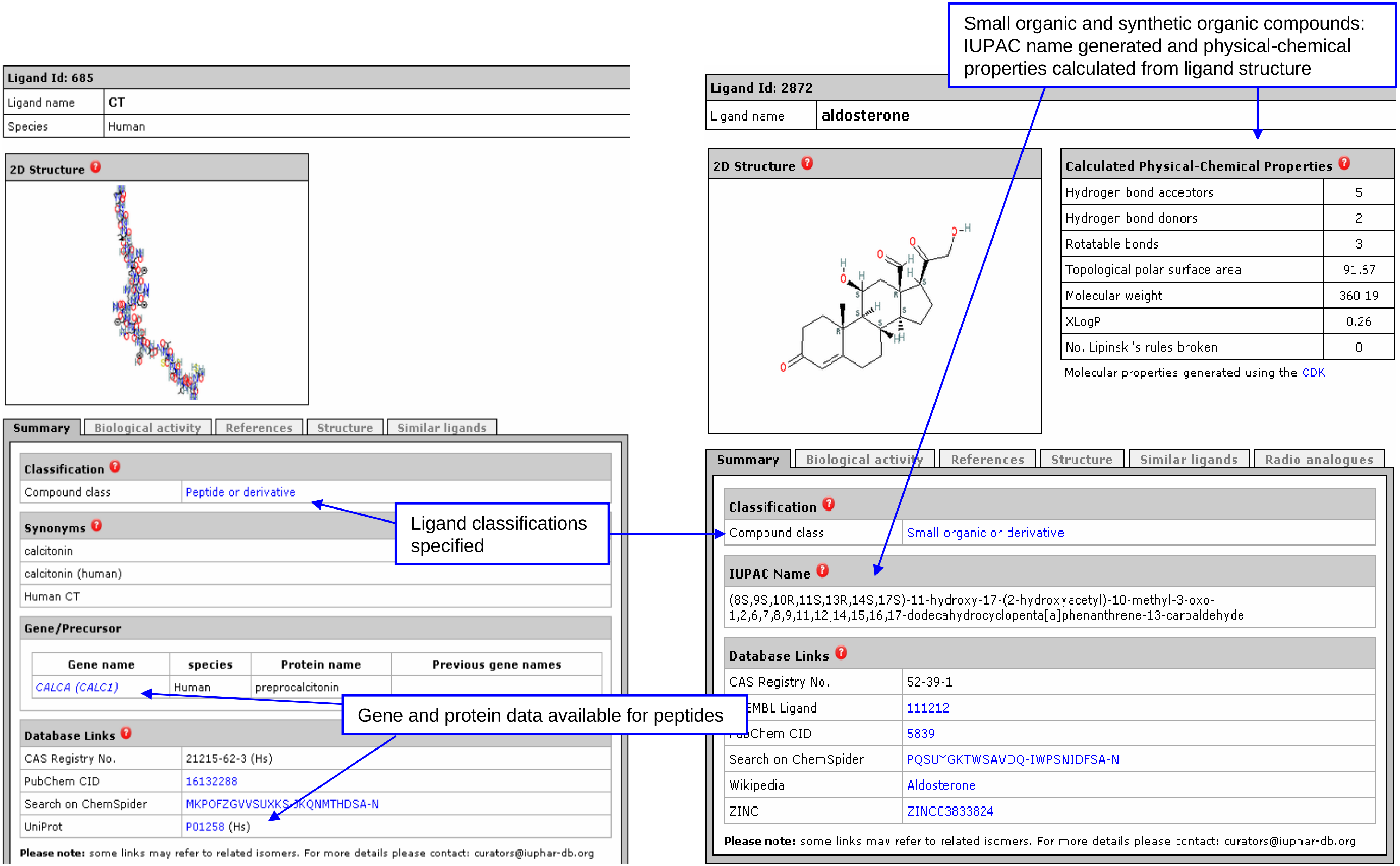
One and three -letter sequences displayed for peptide ligands

Click to search on the **Protein Data Bank** for a protein crystal structure where available

Summary information on post-translational or chemical modifications is provided where relevant

Structural identifiers can be downloaded. See the glossary for more information on these identifiers.

Comparison of ligand pages for a peptide and a small organic



Small organic and synthetic organic compounds: IUPAC name generated and physical-chemical properties calculated from ligand structure

Ligand classifications specified

Gene and protein data available for peptides

Ligand Id: 685	
Ligand name	**CT**
Species	Human

2D Structure

Classification

Compound class	Peptide or derivative

Synonyms

calcitonin

calcitonin (human)

Human CT

Gene/Precursor

Gene name	species	Protein name	Previous gene names
CALCA (CALC1)	Human	preprocalcitonin	

Database Links

CAS Registry No.	21215-62-3 (Hs)
PubChem CID	16132288
Search on ChemSpider	MKPOFZGVVSUXKS-JKQNMTHDSA-N
UniProt	P01258 (Hs)

Please note: some links may refer to related isomers. For more details please contact: curators@iuphar-db.org

Ligand Id: 2872	
Ligand name	**aldosterone**

2D Structure

Calculated Physical-Chemical Properties

Hydrogen bond acceptors	5
Hydrogen bond donors	2
Rotatable bonds	3
Topological polar surface area	91.67
Molecular weight	360.19
XLogP	0.26
No. Lipinski's rules broken	0

Molecular properties generated using the CDK

Classification

Compound class	Small organic or derivative

IUPAC Name

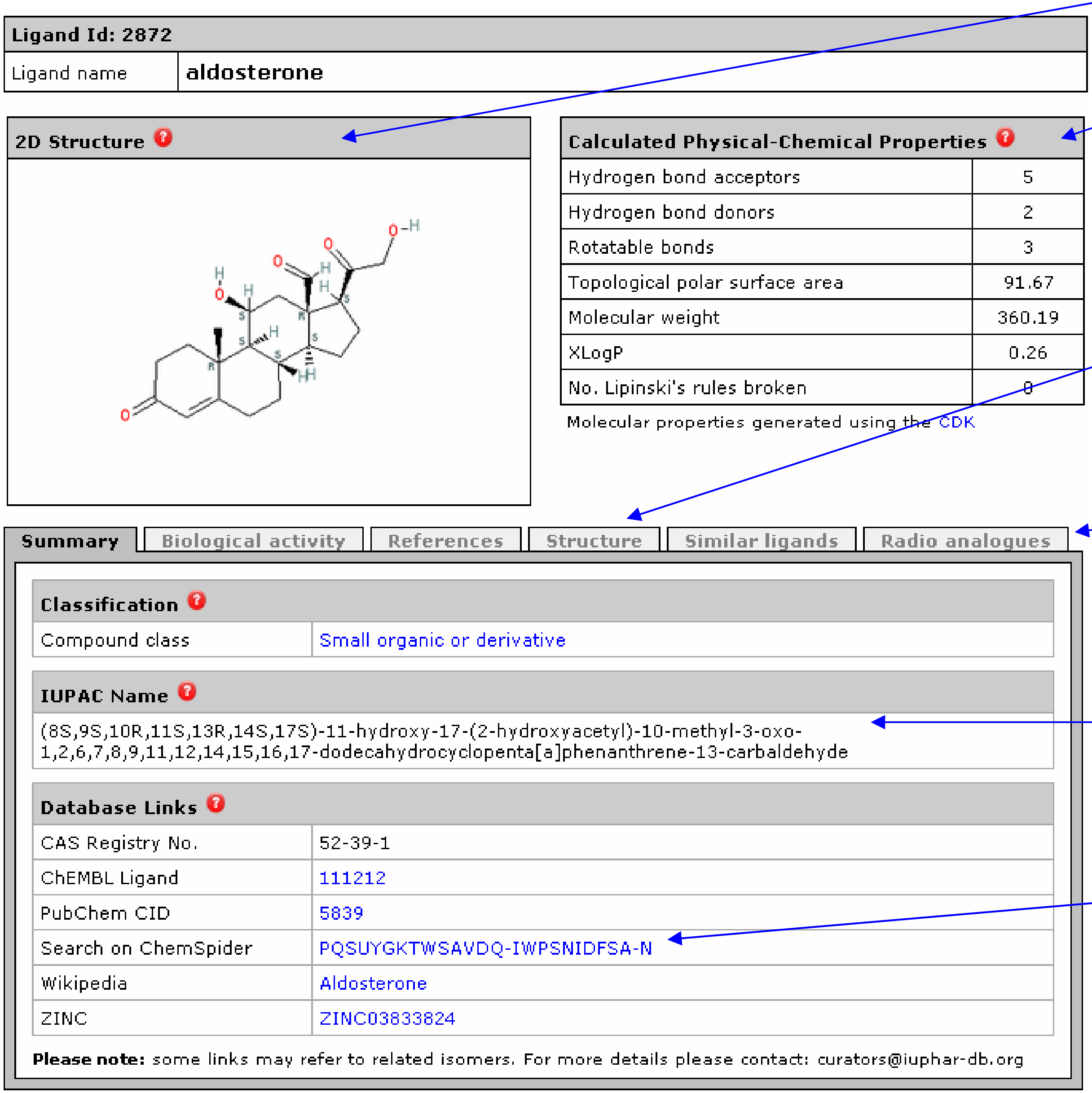
(8S,9S,10R,11S,13R,14S,17S)-11-hydroxy-17-(2-hydroxyacetyl)-10-methyl-3-oxo-1,2,6,7,8,9,11,12,14,15,16,17-dodecahydrocyclopenta[a]phenanthrene-13-carbaldehyde

Database Links

CAS Registry No.	52-39-1
EMBL Ligand	111212
Chem CID	5839
Search on ChemSpider	PQSUYGKTWSAVDQ-IWPSNIDFSA-N
Wikipedia	Aldosterone
ZINC	ZINC03833824

Please note: some links may refer to related isomers. For more details please contact: curators@iuphar-db.org

Example of a small organic ligand page: aldosterone



Ligand Id: 2872	
Ligand name	aldosterone

2D Structure

Calculated Physical-Chemical Properties

Hydrogen bond acceptors	5
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Rotatable bonds	3
Topological polar surface area	91.67
Molecular weight	360.19
XLogP	0.26
No. Lipinski's rules broken	0

Molecular properties generated using the CDK

Classification	
Compound class	Small organic or derivative

IUPAC Name

(8S,9S,10R,11S,13R,14S,17S)-11-hydroxy-17-(2-hydroxyacetyl)-10-methyl-3-oxo-1,2,6,7,8,9,11,12,14,15,16,17-dodecahydrocyclopenta[a]phenanthrene-13-carbaldehyde

Database Links	
CAS Registry No.	52-39-1
ChEMBL Ligand	111212
PubChem CID	5839
Search on ChemSpider	PQSUYGKTWSAVDQ-IWPSNIDFSA-N
Wikipedia	Aldosterone
ZINC	ZINC03833824

Please note: some links may refer to related isomers. For more details please contact: curators@iuphar-db.org

The **2D structure** specifies the ligand stereochemistry

For more information on the **physical-chemical** properties of the molecule, see the glossary

Select **'Structure'** to download structural identifiers for the ligand

Click on '**Radio analogues**' to display (un)labelled variants of the ligand

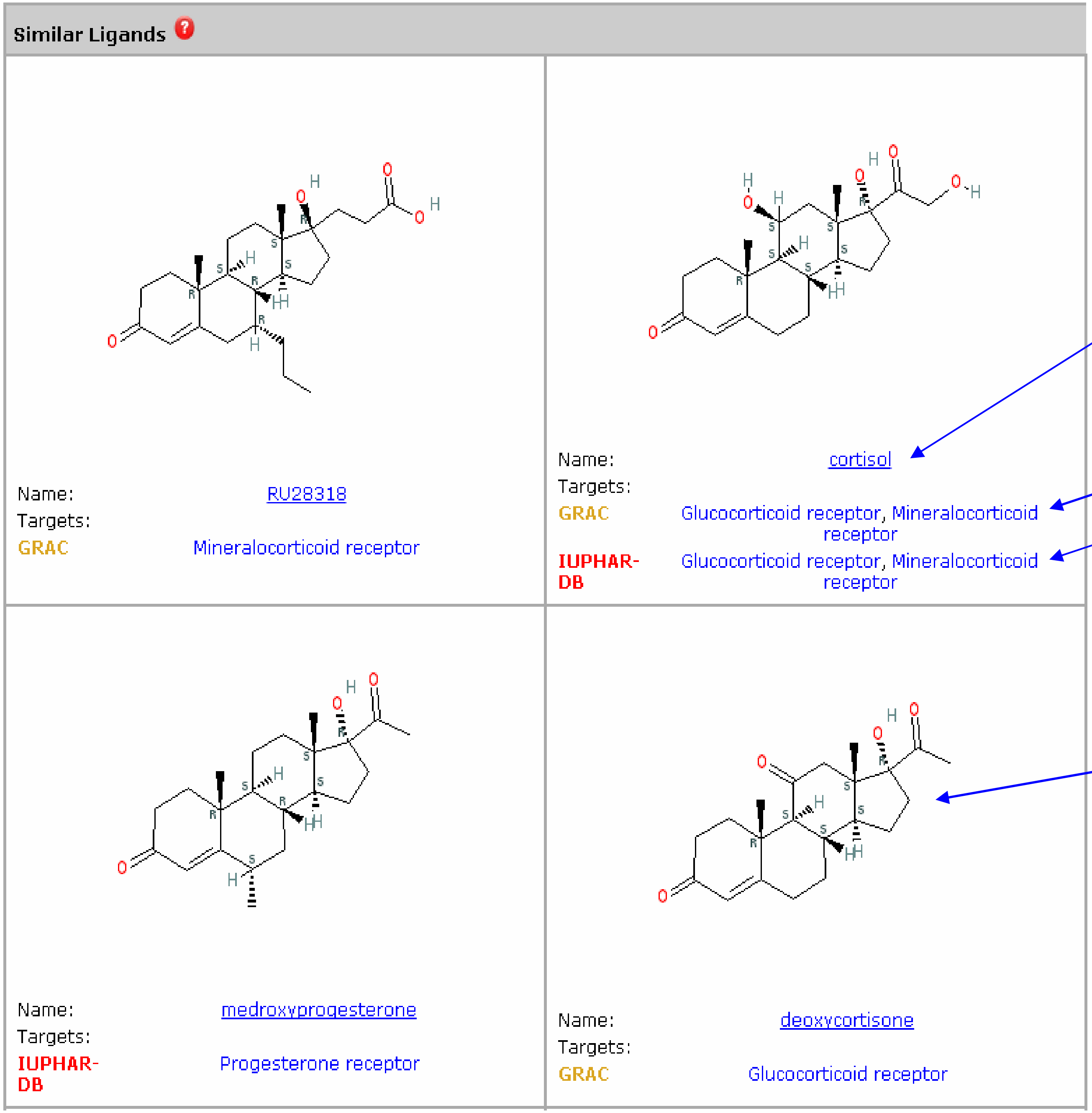
IUPAC name: A systematic chemical name generated according to IUPAC rules

Use the unique **InChi key** to search for the ligand on **ChemSpider.com**

For more information on the GRAC ligand pages see the GRAC help page

Similar ligands:

aldosterone



Name: RU28318
Targets:
GRAC Mineralocorticoid receptor

Name: cortisol
Targets:
GRAC Glucocorticoid receptor, Mineralocorticoid receptor
IUPHAR-DB Glucocorticoid receptor, Mineralocorticoid receptor

Name: medroxyprogesterone
Targets:
IUPHAR-DB Progesterone receptor

Name: deoxycortisone
Targets:
GRAC Glucocorticoid receptor

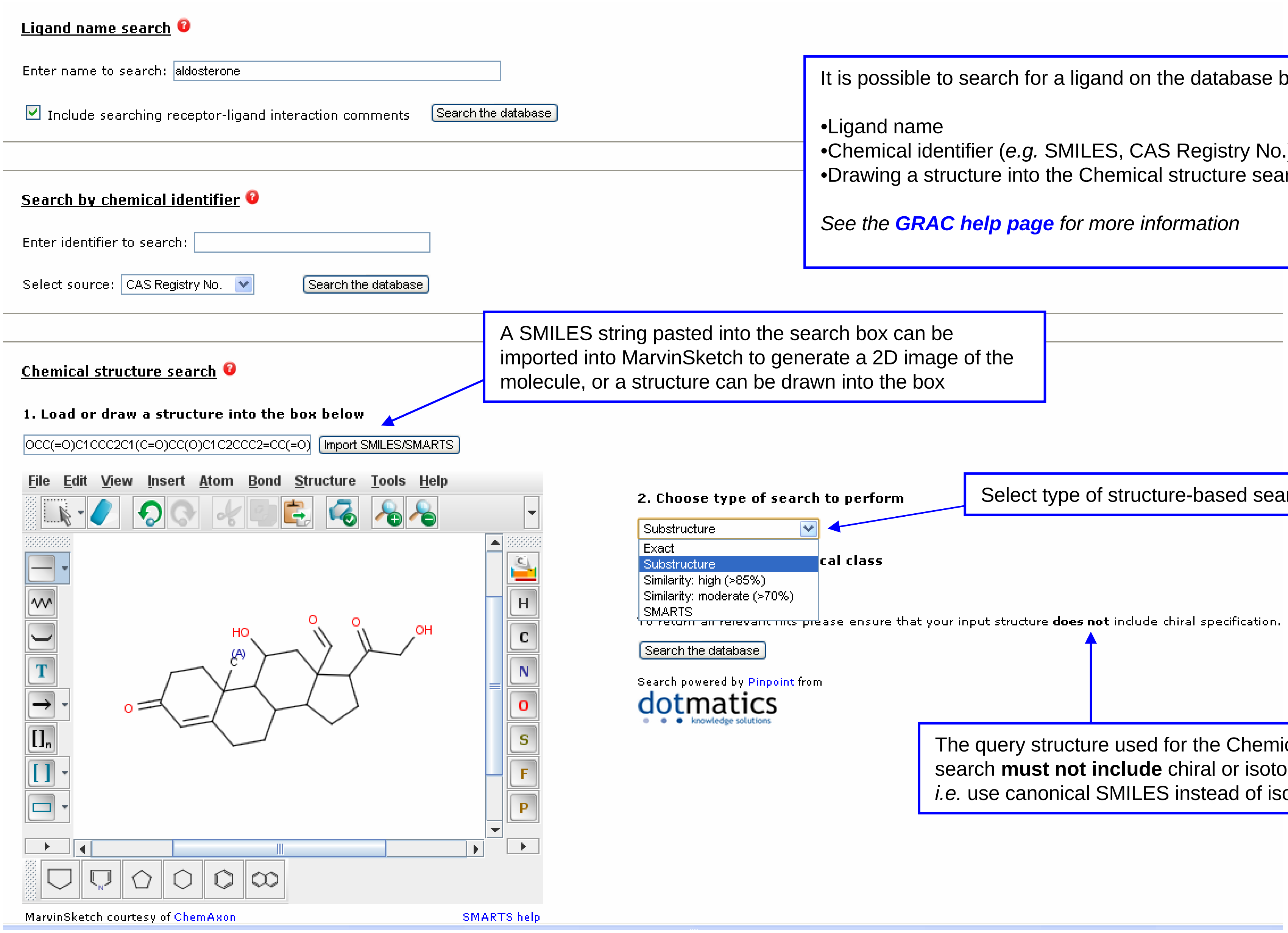
Ligand name: click to link to ligand page

Links to **GRAC** and **IUPHAR** receptor pages with activity data for the ligand

2D image of ligand results, specifying stereochemistry

Advanced search tools: Ligand Search Tools

For a '**quick search**' use the search box on the toolbar



Ligand name search

Enter name to search: aldosterone

☑ Include searching receptor-ligand interaction comments

Search by chemical identifier

Enter identifier to search:

Select source: CAS Registry No.

Chemical structure search

1. Load or draw a structure into the box below

OCC(=O)C1CCC2C1(C=O)CC(O)C1C2CCC2=CC(=O)

2. Choose type of search to perform

Substructure

To return all relevant hits please ensure that your input structure **does not** include chiral specification.

Search powered by Pinpoint from dotmatics

MarvinSketch courtesy of ChemAxon

SMARTS help

It is possible to search for a ligand on the database by:

- Ligand name
- Chemical identifier (*e.g.* SMILES, CAS Registry No.)
- Drawing a structure into the Chemical structure search tool

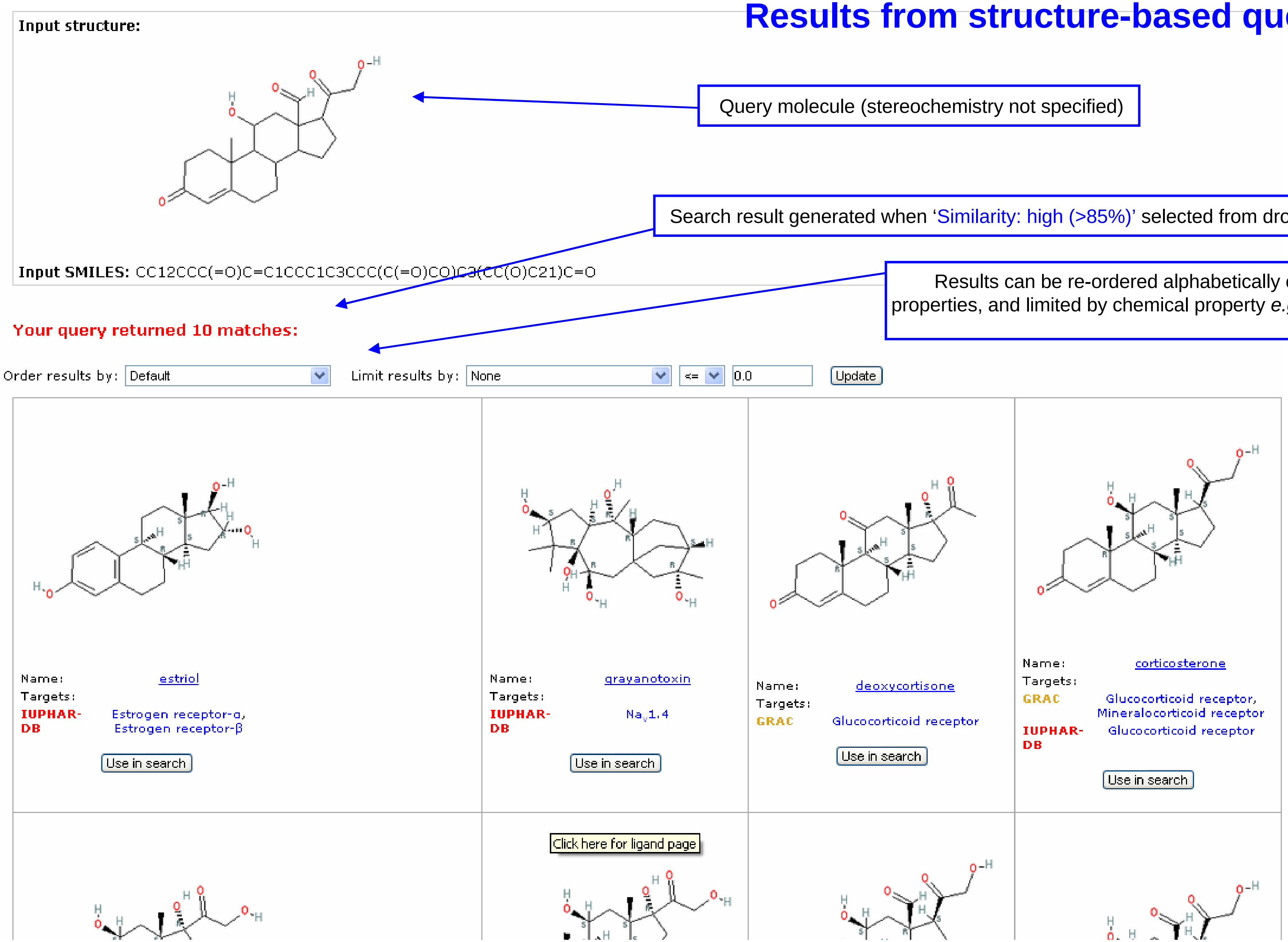
*See the **GRAC help page** for more information*

A SMILES string pasted into the search box can be imported into MarvinSketch to generate a 2D image of the molecule, or a structure can be drawn into the box

Select type of structure-based search to perform

The query structure used for the Chemical Structure search **must not include** chiral or isotopic specification *i.e.* use canonical SMILES instead of isomeric SMILES

Results from structure-based query



Input structure:

Input SMILES: CC12CCC(=O)C=C1CCC1C3CCC(C(=O)CO)C3(CC(O)C21)C=O

Your query returned 10 matches:

Name: estriol Targets: **IUPHAR-DB** Estrogen receptor-α, Estrogen receptor-β	Name: grayanotoxin Targets: **IUPHAR-DB** $\mathrm{Na_v}$1.4	Name: deoxycortisone Targets: **GRAC** Glucocorticoid receptor	Name: corticosterone Targets: **GRAC** Glucocorticoid receptor, Mineralocorticoid receptor **IUPHAR-DB** Glucocorticoid receptor

Query molecule (stereochemistry not specified)

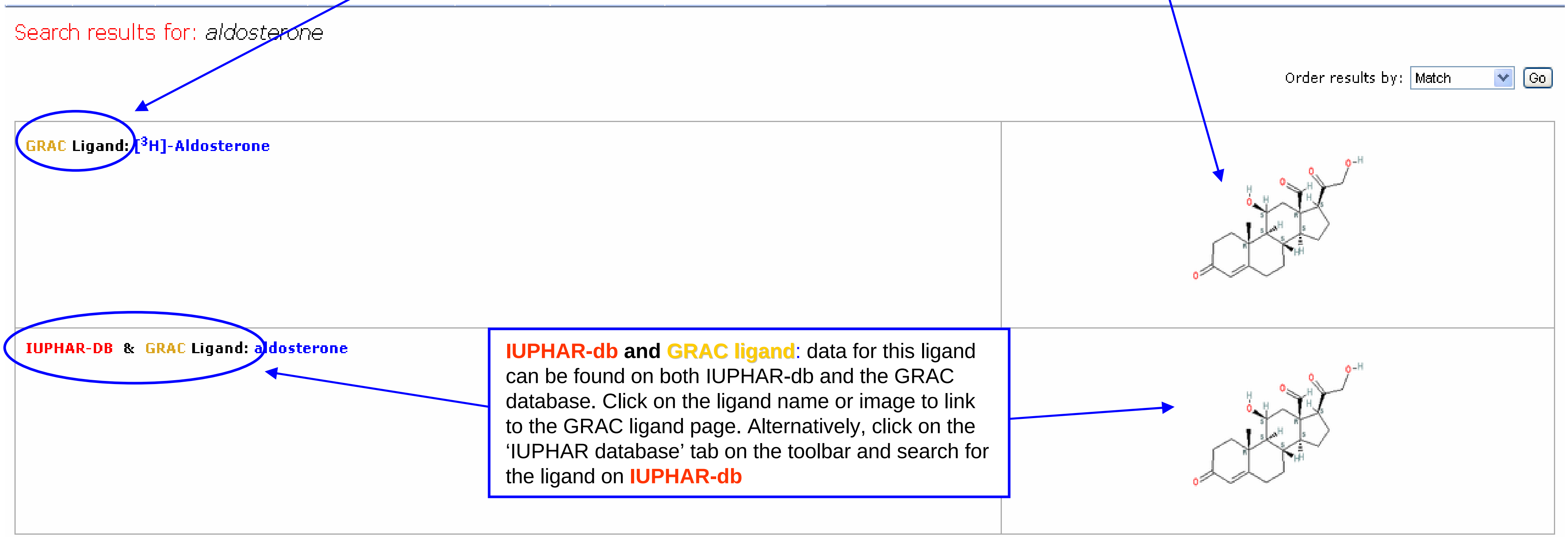
Search result generated when 'Similarity: high (>85%)' selected from drop-down menu

Results can be re-ordered alphabetically or by chemical properties, and limited by chemical property *e.g.* molecular weight

Search results: **Ligand name search-** ‘Aldosterone’

Two results matched by name

GRAC ligand: ligand only available on the GRAC database. Click on the ligand name or ligand image to link to the GRAC ligand page



Search results for: *aldosterone*

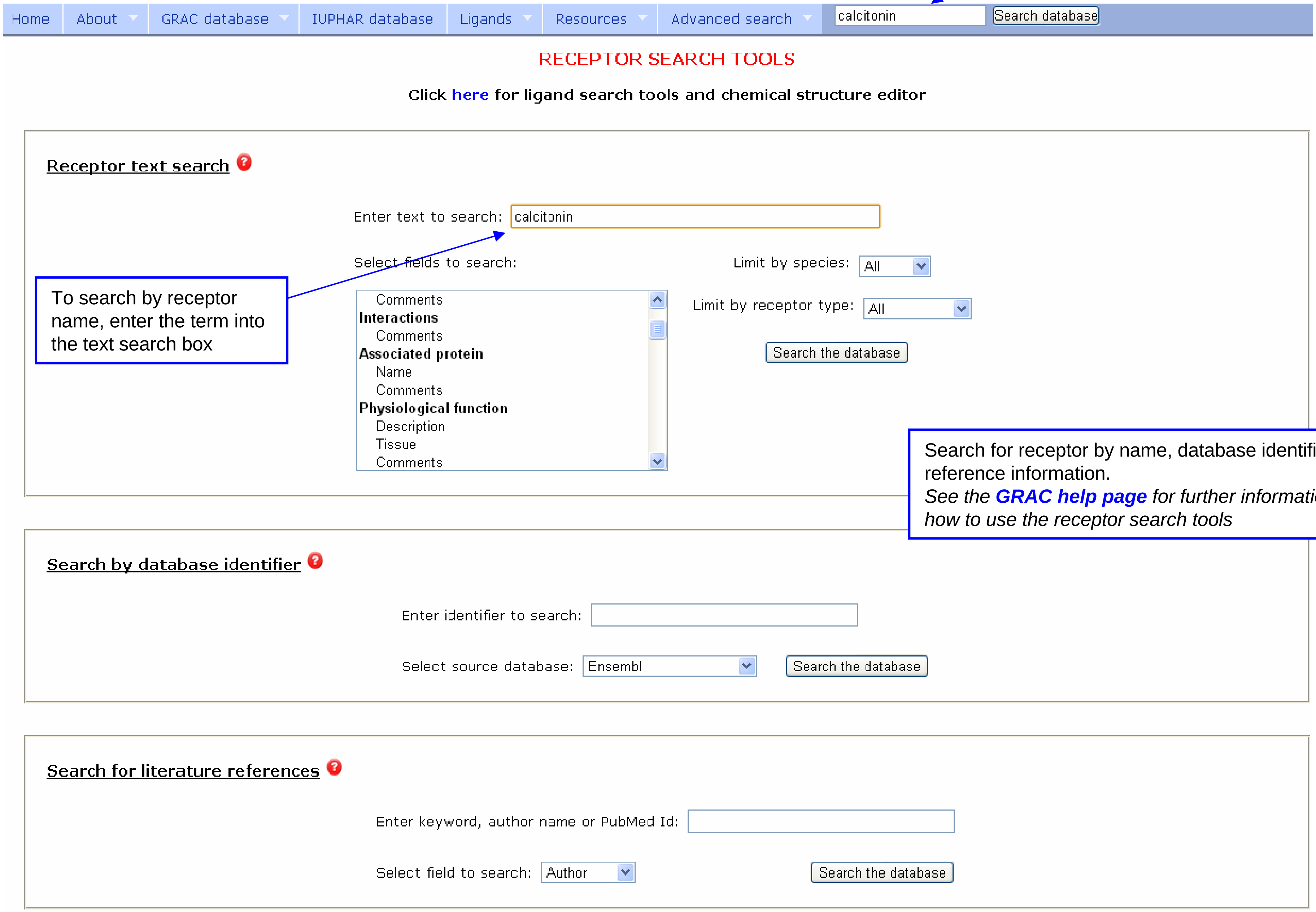
GRAC Ligand: [^{3}H]-Aldosterone

IUPHAR-DB & GRAC Ligand: aldosterone

IUPHAR-db and GRAC ligand: data for this ligand can be found on both IUPHAR-db and the GRAC database. Click on the ligand name or image to link to the GRAC ligand page. Alternatively, click on the ‘IUPHAR database’ tab on the toolbar and search for the ligand on **IUPHAR-db**

Advanced search tools: Receptor Search Tools

*For a '**quick search**' use the search box on the toolbar*



RECEPTOR SEARCH TOOLS

Click here for ligand search tools and chemical structure editor

Receptor text search

Enter text to search: calcitonin

Select fields to search:

Comments
Interactions
Comments
Associated protein
Name
Comments
Physiological function
Description
Tissue
Comments

Limit by species: All

Limit by receptor type: All

Search by database identifier

Enter identifier to search:

Select source database: Ensembl

Search for literature references

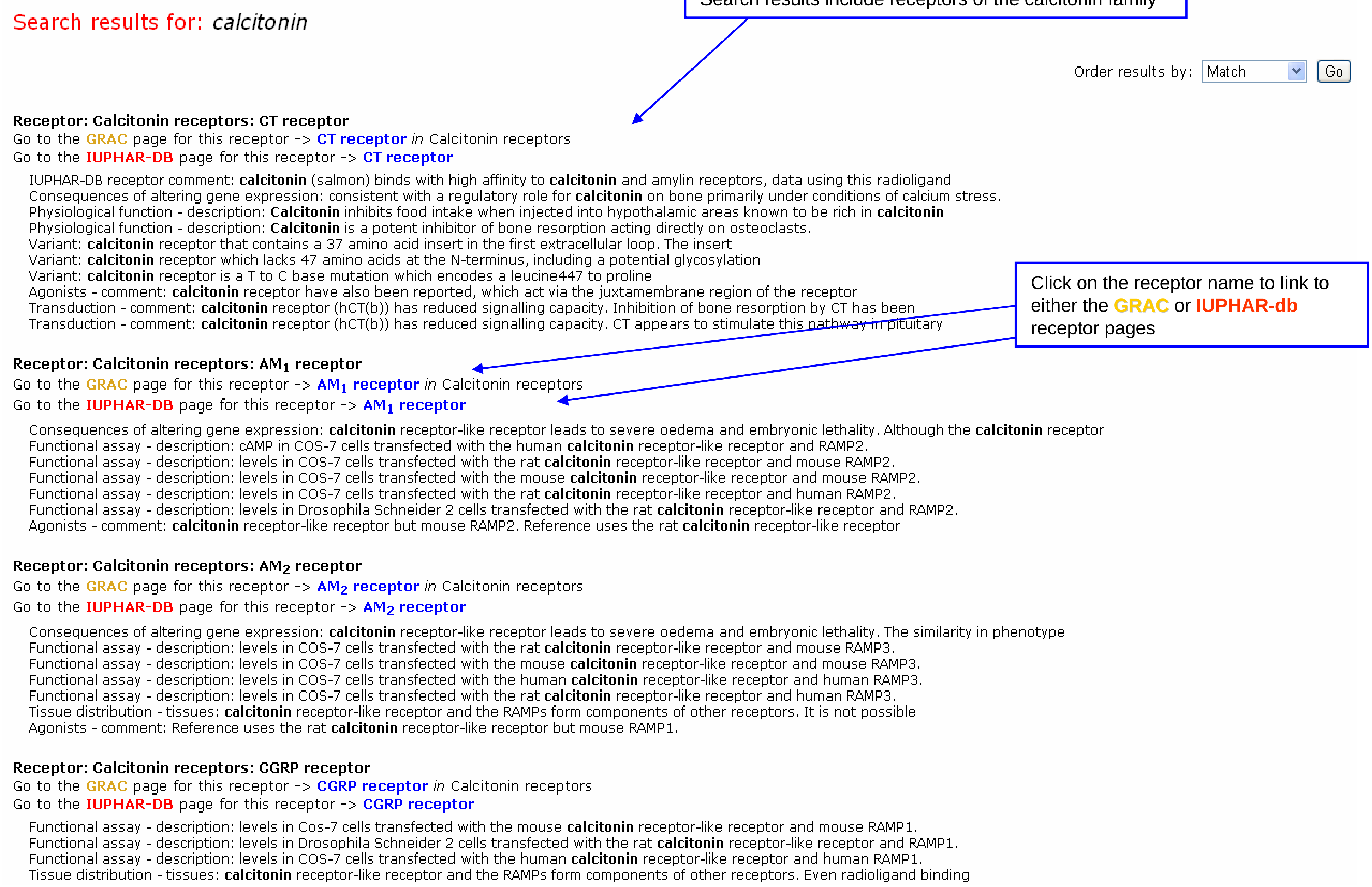
Enter keyword, author name or PubMed Id:

Select field to search: Author

To search by receptor name, enter the term into the text search box

Search for receptor by name, database identifier or reference information.
*See the **GRAC help page** for further information on how to use the receptor search tools*

Receptor search results: calcitonin



Search results include receptors of the calcitonin family

Click on the receptor name to link to either the GRAC or IUPHAR-db receptor pages

Search results for: *calcitonin*

Receptor: Calcitonin receptors: CT receptor
Go to the GRAC page for this receptor -> **CT receptor** *in* Calcitonin receptors
Go to the IUPHAR-DB page for this receptor -> **CT receptor**

IUPHAR-DB receptor comment: **calcitonin** (salmon) binds with high affinity to **calcitonin** and amylin receptors, data using this radioligand
Consequences of altering gene expression: consistent with a regulatory role for **calcitonin** on bone primarily under conditions of calcium stress.
Physiological function - description: **Calcitonin** inhibits food intake when injected into hypothalamic areas known to be rich in **calcitonin**
Physiological function - description: **Calcitonin** is a potent inhibitor of bone resorption acting directly on osteoclasts.
Variant: **calcitonin** receptor that contains a 37 amino acid insert in the first extracellular loop. The insert
Variant: **calcitonin** receptor which lacks 47 amino acids at the N-terminus, including a potential glycosylation
Variant: **calcitonin** receptor is a T to C base mutation which encodes a leucine447 to proline
Agonists - comment: **calcitonin** receptor have also been reported, which act via the juxtamembrane region of the receptor
Transduction - comment: **calcitonin** receptor (hCT(b)) has reduced signalling capacity. Inhibition of bone resorption by CT has been
Transduction - comment: **calcitonin** receptor (hCT(b)) has reduced signalling capacity. CT appears to stimulate this pathway in pituitary

Receptor: Calcitonin receptors: AM$_1$ receptor
Go to the GRAC page for this receptor -> **AM$_1$ receptor** *in* Calcitonin receptors
Go to the IUPHAR-DB page for this receptor -> **AM$_1$ receptor**

Consequences of altering gene expression: **calcitonin** receptor-like receptor leads to severe oedema and embryonic lethality. Although the **calcitonin** receptor
Functional assay - description: cAMP in COS-7 cells transfected with the human **calcitonin** receptor-like receptor and RAMP2.
Functional assay - description: levels in COS-7 cells transfected with the rat **calcitonin** receptor-like receptor and mouse RAMP2.
Functional assay - description: levels in COS-7 cells transfected with the mouse **calcitonin** receptor-like receptor and mouse RAMP2.
Functional assay - description: levels in COS-7 cells transfected with the rat **calcitonin** receptor-like receptor and human RAMP2.
Functional assay - description: levels in Drosophila Schneider 2 cells transfected with the rat **calcitonin** receptor-like receptor and RAMP2.
Agonists - comment: **calcitonin** receptor-like receptor but mouse RAMP2. Reference uses the rat **calcitonin** receptor-like receptor

Receptor: Calcitonin receptors: AM$_2$ receptor
Go to the GRAC page for this receptor -> **AM$_2$ receptor** *in* Calcitonin receptors
Go to the IUPHAR-DB page for this receptor -> **AM$_2$ receptor**

Consequences of altering gene expression: **calcitonin** receptor-like receptor leads to severe oedema and embryonic lethality. The similarity in phenotype
Functional assay - description: levels in COS-7 cells transfected with the rat **calcitonin** receptor-like receptor and mouse RAMP3.
Functional assay - description: levels in COS-7 cells transfected with the mouse **calcitonin** receptor-like receptor and mouse RAMP3.
Functional assay - description: levels in COS-7 cells transfected with the human **calcitonin** receptor-like receptor and human RAMP3.
Functional assay - description: levels in COS-7 cells transfected with the rat **calcitonin** receptor-like receptor and human RAMP3.
Tissue distribution - tissues: **calcitonin** receptor-like receptor and the RAMPs form components of other receptors. It is not possible
Agonists - comment: Reference uses the rat **calcitonin** receptor-like receptor but mouse RAMP1.

Receptor: Calcitonin receptors: CGRP receptor
Go to the GRAC page for this receptor -> **CGRP receptor** *in* Calcitonin receptors
Go to the IUPHAR-DB page for this receptor -> **CGRP receptor**

Functional assay - description: levels in Cos-7 cells transfected with the mouse **calcitonin** receptor-like receptor and mouse RAMP1.
Functional assay - description: levels in Drosophila Schneider 2 cells transfected with the rat **calcitonin** receptor-like receptor and RAMP1.
Functional assay - description: levels in COS-7 cells transfected with the human **calcitonin** receptor-like receptor and human RAMP1.
Tissue distribution - tissues: **calcitonin** receptor-like receptor and the RAMPs form components of other receptors. Even radioligand binding

Glossary of terms used in Guide to PHARMACOLOGY

Ligand classifications	
Synthetic organics	Low molecular weight, non-polymeric compounds produced via either total synthesis or semi-synthetic processes
Small organics	Low molecular weight, non-peptidic, biogenic compounds produced by life processes (normally endogenous and of animal origin) and their close analogues
Natural products	Non-peptidic, biogenic compounds derived from living organisms and their close synthetic derivatives
Peptides	Synthetic, semi-synthetic and natural peptides (oligopeptides and cyclic peptides)
Inorganics	Ions and other inorganic compounds
Others	Silicones and other non-carbon containing molecules and polymers
Ligand structural information and properties	
SMILES	(Simplified Molecular Input Line Entry Specification) A specification for unambiguously describing the structure of chemical molecules using short ASCII strings
Canonical SMILES	SMILES specify a unique representation of the 2D structure without chiral or isotopic specifications
Isomeric SMILES	SMILES include chiral specification
InChI standard identifier	(IUPAC International Chemical Identifier) InChI is a non-proprietary, standard, textual identifier for chemical substances designed to facilitate linking of information and database searching
InChI standard key	An InChI Key is a simplified version of a full InChI, designed for easier web searching
Calculated Physical-Chemical Properties	Calculated molecular properties are available for small molecules and natural products (not peptides). Properties were generated using the CDK Toolkit. All properties were selected to enable the prediction of the Lipinski Rule-of-Five profile or ‘druglikeness’ for each ligand
Receptor information	
Nomenclature	The recommended nomenclature for a structurally and operationally distinct receptor in a given family. Where this is the NC-IUPHAR published recommended nomenclature, this is specified in the Overview section with references to the relevant articles in *Pharmacological Reviews*. In cases where there are no published NC-IUPHAR recommendations, the adopted nomenclature is usually one of: the HGNC approved gene name, a name commonly used in the literature or a preliminary recommendation from NC-IUPHAR.
Principal transduction	The primary G proteins that the GPCR couples to, where established
Functional Characteristics	Provides details of the conductance, voltage-dependence, rectification and selectivity properties of ion channels
Hs, Mm, Rn	Indicates the species of the receptor. Hs: *Homo sapiens*; Mm: *Mus musculus*; Rn: *Rattus norvegicus*

Glossary of terms used in Guide to PHARMACOLOGY

Experimental measures of ligand action	
EC_{50}	The molar concentration of an agonist that produces 50% of the maximal possible effect of that agonist. Other percentage values (EC_{20}, EC_{40}, etc.) can be specified. The action of the agonist may be stimulatory or inhibitory
IC_{50}	This term is used in a number of ways: (*i*) the molar concentration of an antagonist that reduces the response to an agonist by 50%; the concentration of agonist should be given; (*ii*) the molar concentration of an unlabeled agonist or antagonist that inhibits the binding of a radioligand by 50%; the concentration of radioligand should be given; (*iii*) the molar concentration of an inhibitory agonist that reduces a response by 50% of the maximal inhibition that can be attained; this latter usage is not recommended- instead the term, EC_{50}, should be used since this is an agonist effect
K_B	K_B refers to the equilibrium dissociation constant of a ligand (traditionally, a competitive antagonist) determined by means of a functional assay
K_d	K_d refers to the equilibrium dissociation constant of a ligand determined directly in a binding assay using a labeled form of the ligand
K_i	K_i refers to the equilibrium dissociation constant of a ligand determined in inhibition studies. The K_i for a given ligand is typically (but not necessarily) determined in a competitive radioligand binding study by measuring the inhibition of the binding of a reference radioligand by the competing ligand of interest under equilibrium conditions
pA_2	The negative logarithm to base 10 of the molar concentration of an antagonist that makes it necessary to double the concentration of the agonist needed to elicit the original submaximal response obtained in the absence of antagonist
pEC_{50}	The negative logarithm to base 10 of the EC_{50} of an agonist
pIC_{50}	The negative logarithm to base 10 of the IC_{50} of an agonist or antagonist
pK_B	The negative logarithm to base 10 of the K_B
pK_d	The negative logarithm to base 10 of the K_d
pK_i	The negative logarithm to base 10 of the K_i
Concentration range	Where affinity data are not available, the concentration range of ligand used for the study is displayed (in M)
Rank order of potency	The order of potency of the activity of a series of ligands at a particular receptor